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* * * * * Welcome to STN International * * * * *

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NEWS	23	AUG 15	CAOLD to be discontinued on December 31, 2008
NEWS	24	AUG 15	CAPLUS currency for Korean patents enhanced
NEWS	25	AUG 25	CA/CAPLUS, CASREACT, and IFI and USPAT databases enhanced for more flexible patent number searching
NEWS	26	AUG 27	CAS definition of basic patents expanded to ensure comprehensive access to substance and sequence information

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* * * * * STN Columbus * * * * *

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=> file caplus

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FULL ESTIMATED COST	0.21	0.21

FILE 'CAPLUS' ENTERED AT 11:51:25 ON 08 SEP 2008

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FILE COVERS 1907 - 8 Sep 2008 VOL 149 ISS 11

FILE LAST UPDATED: 7 Sep 2008 (20080907/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

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(JP0734755/PN)

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=> s 5962455/pn

L3 0 5962455/PN

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L4 1 US5962455/PN

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L2 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN

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 663 SEH
 (SEH OR SEHS)
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 30226 EPOXIDES
 67936 EPOXIDE
 (EPOXIDE OR EPOXIDES)
 24872 HYDROLASE
 9348 HYDROLASES
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 (HYDROLASE OR HYDROLASES)
 2959 EPOXIDE HYDROLASE
 (EPOXIDE(W)HYDROLASE)
 L6 28 L5 AND (SEH OR EPOXIDE HYDROLASE)

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(FILE 'HOME' ENTERED AT 11:50:56 ON 08 SEP 2008)

FILE 'CAPLUS' ENTERED AT 11:51:25 ON 08 SEP 2008

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 L2 1 S JP07304755/PN
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 L6 28 S L5 AND (SEH OR EPOXIDE HYDROLASE)

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=> s l7 and (seh or epoxide hydrolase)

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663 SEH
10 SEHS
663 SEH
      (SEH OR SEHS)
52008 EPOXIDE
30226 EPOXIDES
67936 EPOXIDE
      (EPOXIDE OR EPOXIDES)
24872 HYDROLASE
9348 HYDROLASES
29509 HYDROLASE
      (HYDROLASE OR HYDROLASES)
2959 EPOXIDE HYDROLASE
      (EPOXIDE(W)HYDROLASE)
L8 31 L7 AND (SEH OR EPOXIDE HYDROLASE)

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=> d his

(FILE 'HOME' ENTERED AT 11:50:56 ON 08 SEP 2008)

FILE 'CAPLUS' ENTERED AT 11:51:25 ON 08 SEP 2008

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L1 0 S JP 0734755/PN
L2 1 S JP07304755/PN
L3 0 S 5962455/PN
L4 1 S US5962455/PN
      SELECT L2 1 RN

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L5      74206 S E1-E117
L6      28 S L5 AND (SEH OR EPOXIDE HYDROLASE)
        SELECT L4 1 RN
L7      80303 S E1-E135
L8      31 S L7 AND (SEH OR EPOXIDE HYDROLASE)

```

```

=> focus l6 or l8
OR IS NOT VALID HERE
The term is either unrecognized or invalid.

```

```

=> foluc l6
FOLUC IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

```

```

=> folcu l6
FOLCU IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

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=> focus l6
PROCESSING COMPLETED FOR L6
L9      28 FOCUS L6 1-

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=> focus l8
PROCESSING COMPLETED FOR L8
L10     31 FOCUS L8 1-

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=> d ibib abs hitstr 1-28 l9

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L9  ANSWER 1 OF 28  CAPLUS  COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER:      2006:386356  CAPLUS
DOCUMENT NUMBER:       144:427964
TITLE:                 Multiple pharmacophore-containing inhibitors for
                        soluble epoxide hydrolase and
                        disease treatment
INVENTOR(S):           Hammock, Bruce D.; Kim, In-Hae; Morisseau, Christophe;
                        Watanabe, Takaho; Newman, John W.
PATENT ASSIGNEE(S):    The Regents of the University of California, USA
SOURCE:                PCT Int. Appl., 179 pp.
                        CODEN: PIXXD2
DOCUMENT TYPE:         Patent
LANGUAGE:              English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006045119	A2	20060427	WO 2005-US38282	20051020
WO 2006045119	A9	20060526		
WO 2006045119	A3	20070208		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,				
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GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,				
LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ,				
NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,				
SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN,				
YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,				

IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
 CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
 GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM

AU 2005295167	A1	20060427	AU 2005-295167	20051020
CA 2584342	A1	20060427	CA 2005-2584342	20051020
US 20060270609	A1	20061130	US 2005-256685	20051020
EP 1814875	A2	20070808	EP 2005-817420	20051020

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
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 BA, HR, MK, YU

CN 101084216	A	20071205	CN 2005-80043035	20051020
JP 2008517072	T	20080522	JP 2007-538151	20051020
IN 2007KN01641	A	20070817	IN 2007-KN1641	20070508

PRIORITY APPLN. INFO.: US 2004-651487P P 20041020
 WO 2005-US38282 W 20051020

OTHER SOURCE(S): MARPAT 144:427964

AB Inhibitors of the soluble epoxide hydrolase (sEH
) are provided that incorporate multiple pharmacophores and are useful in
 the treatment of diseases such as hypertension and inflammation. Thus,
 hundreds of inhibitors were synthesized and tested as inhibitors of human
 and mouse sEH. The pharmacokinetics of various inhibitors was
 also studied.

IT 75-03-6, Ethyl iodide 75-30-9, Isopropyl iodide
 100-39-0, Benzyl bromide
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (multiple pharmacophore-containing inhibitors for soluble epoxide
 hydrolase and disease treatment)

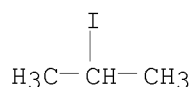
RN 75-03-6 CAPLUS

CN Ethane, iodo- (CA INDEX NAME)

H₃C-CH₂-I

RN 75-30-9 CAPLUS

CN Propane, 2-iodo- (CA INDEX NAME)



RN 100-39-0 CAPLUS

CN Benzene, (bromomethyl)- (CA INDEX NAME)

Ph-CH₂-Br

L9 ANSWER 2 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:764736 CAPLUS

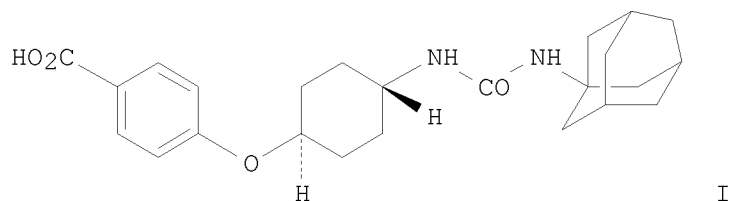
DOCUMENT NUMBER: 147:343722

TITLE: Orally Bioavailable Potent Soluble Epoxide
 Hydrolase Inhibitors

AUTHOR(S): Hwang, Sung Hee; Tsai, Hsing-Ju; Liu, Jun-Yan;
 Morisseau, Christophe; Hammock, Bruce D.

CORPORATE SOURCE: Department of Entomology and UCD Cancer Center,
 University of California, Davis, CA, 95616-8584, USA

SOURCE: Journal of Medicinal Chemistry (2007), 50(16),
3825-3840
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 147:343722
GI



AB A series of N,N'-disubstituted ureas having a conformationally restricted cis- or trans-1,4-cyclohexane α to the urea were prepared and tested as soluble epoxide hydrolase (sEH) inhibitors. This series of compds. showed low nanomolar to picomolar activities against recombinant human sEH. Both isomers showed similar potencies, but the trans isomers were more metabolically stable in human hepatic microsomes. Furthermore, these new potent inhibitors show a greater metabolic stability in vivo than previously described sEH inhibitors. Trans-4-[4-(3-adamantan-1-ylureido)cyclohexyloxy]benzoic acid (I, t-AUCB, IC₅₀ = 1.3 \pm 0.05 nM) had excellent oral bioavailability (98%, n = 2) and blood area under the curve in dogs and was effective in vivo to treat hypotension in lipopolysaccharide challenged murine models.

IT 100-39-0, Benzyl bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of cis and trans isomers of (adamantan-1-ylureido)cyclohexanol derivs. as orally bioavailable potent soluble epoxide hydrolase inhibitors)

RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)

Ph-CH₂-Br

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:644048 CAPLUS

DOCUMENT NUMBER: 147:72748

TITLE: Substituted pyrazole compounds useful as soluble epoxide hydrolase inhibitors and their preparation and pharmaceutical compositions

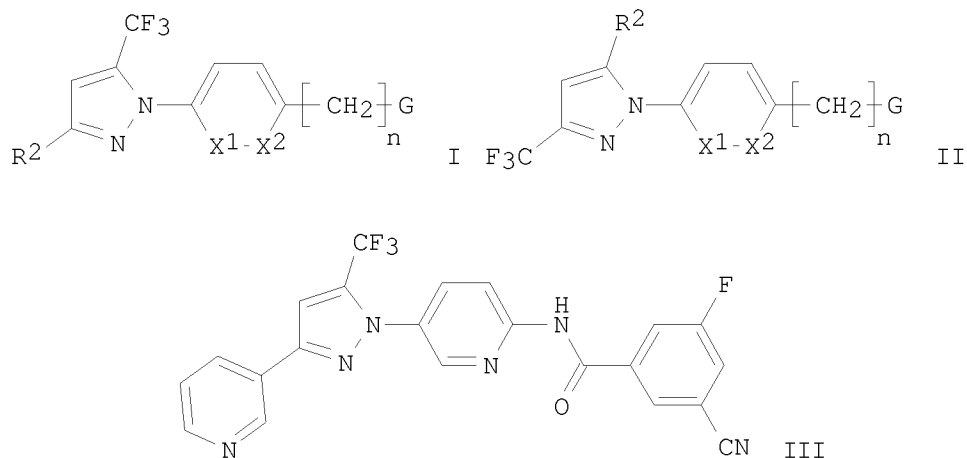
INVENTOR(S): Fleck, Roman Wolfgang; Guo, Xin; Lo, Ho Yin; Man, Chuk Chui

PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.

SOURCE: PCT Int. Appl., 317pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007067836	A2	20070614	WO 2006-US60863	20061114
WO 2007067836	A3	20071115		
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AB Disclosed are compds. of formula I and II that are active against soluble epoxide hydrolase (sEH), compns. thereof and methods of using and making same. Compds. of formula I and II where G is acylamino; X₁-X₂ s CH=CH, N=CH, C=N, and N=N; R₂ is (un)substituted heteroaryl and (un)substituted carbocycles; n is 0 - 5; and their pharmaceutically acceptable salts thereof, are claimed. Example compound III was prepared by acylation of 3-acetylpyridine with Et trifluoroacetate; the resulting 4,4,4-trifluoro-1-(pyridin-3-yl)butane-1,3-dione underwent cyclization with 2-fluoro-5-hydrazinopyridine to give 2-(6-fluoropyridin-3-yl)-5-(pyridin-3-yl)-3-trifluoromethyl-3,4-dihydro-2H-pyrazol-3-ol, which

underwent amination and elimination to give 5-(3-(pyridin-3-yl)-5-trifluoromethylpyrazol-1-yl)pyridin-2-ylamine, which underwent amidation with 3-cyano-5-fluorobenzoic acid to give compound III. All the invention compds. were evaluated for their sEH inhibitory activity.

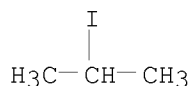
IT 75-30-9, 2-Iodopropane

RL: RCT (Reactant); RACT (Reactant or reagent)

(starting material; preparation of substituted pyrazole compds. useful as soluble epoxide hydrolase inhibitors)

RN 75-30-9 CAPLUS

CN Propane, 2-iodo- (CA INDEX NAME)



L9 ANSWER 4 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1061416 CAPLUS

DOCUMENT NUMBER: 147:385844

TITLE: Preparation of heterocyclic urea derivatives particularly piperidinyl ureas as inhibitors of soluble epoxide hydrolase for the treatment of hypertension, inflammation and other diseases

INVENTOR(S): Hammock, Bruce D.; Jones, Paul D.; Morisseau, Christophe; Huang, Huazhang; Tsai, Hsing-Ju; Gless, Richard, Jr.

PATENT ASSIGNEE(S): The Regents of the University of California, USA; Arete Therapeutics

SOURCE: PCT Int. Appl., 116pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

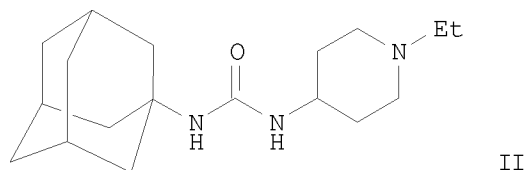
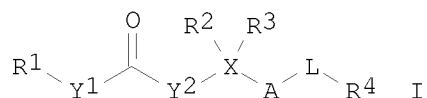
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2007106525	A1	20070920	WO 2007-US6412	20070313
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RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

US 20070225283 A1 20070927 US 2007-685674 20070313

PRIORITY APPLN. INFO.: US 2006-782172P P 20060313

OTHER SOURCE(S): MARPAT 147:385844

GI



AB Title compds. I [R1 = (un)substituted alkyl, arylalkyl, cycloalkyl or heterocyclyl; Y1 = bond, C(R5)2, NR5 or O; Y2 = bond, NR5 and O; X = (CH2)n, wherein n = 0-1; R2, R3 and R5 independently = H, alkyl or COR6, wherein R6 = H, OH, NH2, alkyl or alkoxy; R4 = H, (un)substituted (hetero)alkyl, alkenyl, alkynyl, arylalkyl, cycloalkyl or heterocyclyl; A = (un)substituted heterocyclyl; L = direct bond, (hetero)alkylene, cycloalkylene, (hetero)arylene, CO, Se or SOm, wherein m = 0-2], and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of soluble epoxide hydrolase (sEH). Thus, e.g., II was prepared by the reaction of 4-aminopiperidine with benzaldehyde and further protection with BOC-anhydride to provide intermediate carbamate which underwent acylation with 1-adamantyl isocyanate followed by deprotection and alkylation with bromoethane. I have an IC50 value against sEH of ≤ 150 nM. As inhibitors of sEH, I should prove useful for the treatment of hypertension, inflammation, adult respiratory distress syndrome, diabetic complications, end stage renal disease, Raynaud syndrome and arthritis. The invention also disclosed a cis-epoxyeicosantrienoic acid (EET) which can be administered with the sEH inhibitor (no data).

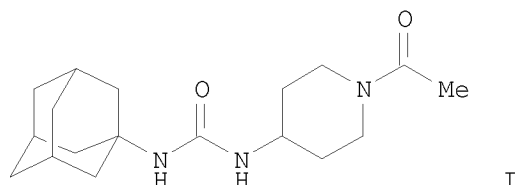
IT 100-39-0, Benzylbromide
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of heterocyclic urea derivs. particularly piperidinyl ureas as inhibitors of soluble epoxide hydrolase for the treatment of hypertension, inflammation and other diseases)
 RN 100-39-0 CAPLUS
 CN Benzene, (bromomethyl)- (CA INDEX NAME)

Ph-CH₂-Br

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2006:874483 CAPLUS
 DOCUMENT NUMBER: 145:454915
 TITLE: Synthesis and SAR of conformationally restricted inhibitors of soluble epoxide hydrolase
 AUTHOR(S): Jones, Paul D.; Tsai, Hsing-Ju; Do, Zung N.; Morisseau, Christophe; Hammock, Bruce D.
 CORPORATE SOURCE: Department of Entomology and Cancer Research Center, University of California, Davis, CA, 95616, USA
 SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(19), 5212-5216

PUBLISHER:	CODEN: BMCLE8; ISSN: 0960-894X
DOCUMENT TYPE:	Elsevier Ltd.
LANGUAGE:	Journal
OTHER SOURCE(S):	English
GI	CASREACT 145:454915



AB A series of conformationally restricted inhibitors of human soluble epoxide hydrolase (sEH) was synthesized. Inhibition potency of the described compds. was studied against recombinant sEH. N-(1-Acetylpiperidin-4-yl)-N'-(adamant-1-yl)urea (I) was found to be a potent inhibitor that was also orally bioavailable in canines.

IT 100-39-0, Benzyl bromide
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation, soluble epoxide hydrolase inhibiting activity, SAR and pharmacokinetics of (N-adamantyl-N'-piperidinyl)urea derivs. using alkylation and acylation of (N-adamantyl-N'-piperidinyl)urea hydrochloride as key steps)

RN 100-39-0 CAPLUS

CN Benzene, (bromomethyl)- (CA INDEX NAME)

Ph-CH₂-Br

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:1245497 CAPLUS

DOCUMENT NUMBER: 146:92622

TITLE: Design of bioavailable derivatives of 12-(3-adamantan-1-yl-ureido)dodecanoic acid, a potent inhibitor of the soluble epoxide hydrolase

AUTHOR(S): Kim, In-Hae; Nishi, Kosuke; Tsai, Hsing-Ju; Bradford, Tanya; Koda, Yasuko; Watanabe, Takaho; Morisseau, Christophe; Blanchfield, Joanne; Toth, Istvan; Hammock, Bruce D.

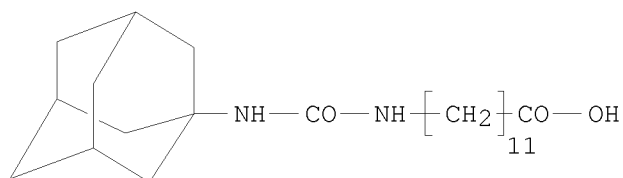
CORPORATE SOURCE: Department of Entomology and University of California Davis Cancer Center, University of California, Davis, CA, 95616, USA

SOURCE: Bioorganic & Medicinal Chemistry (2007), 15(1), 312-323
 CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English
 OTHER SOURCE(S): CASREACT 146:92622
 GI



I

AB The soluble epoxide hydrolase (sEH) plays an important role in the metabolism of endogenous chemical mediators involved in blood pressure regulation and vascular inflammation. 12-(3-Adamantan-1-yl-ureido)-dodecanoic acid (AUDA, I) is a very active inhibitor of sEH both in vitro and in vivo. However, its relatively high m.p. and limited solubility in either water or oil-based solvents leads to difficulties in formulating the compound and often results in poor in vivo availability. We investigated the effect of derivatization of the acid functional group of inhibitor I on the inhibition potencies, phys. properties, and pharmacokinetic properties. For human sEH, similar inhibition potency was obtained when the acid of compound I was modified to esters. The resulting compds. exhibited improved phys. properties (23-66°C lower m.p. and 5-fold better solubility in oil). Pharmacokinetic studies showed that the esters possess improved oral bioavailability in mice. On the other hand, amide derivs. of I did not show significant improvement in inhibition potencies or phys. properties (higher m.ps. and lower solubility). The esterification of I results in compds. that are easier to formulate in animal food and in triglycerides for gavage and other routes of administration, making it easier to study the biol. effects of sEH inhibition in vivo.

IT 100-39-0, Benzyl bromide 106-95-6, Allyl bromide, reactions
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (bioavailable derivs. of (adamantany lureido)dodecanoic acid as inhibitors of soluble epoxide hydrolase)

RN 100-39-0 CAPLUS
 CN Benzene, (bromomethyl)- (CA INDEX NAME)

Ph-CH₂-Br

RN 106-95-6 CAPLUS
 CN 1-Propene, 3-bromo- (CA INDEX NAME)

Br-CH₂-CH=CH₂

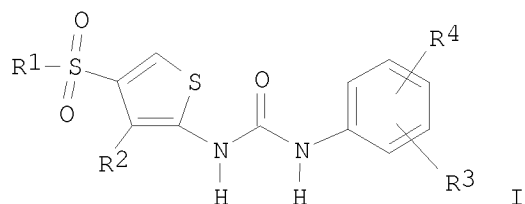
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:433827 CAPLUS
DOCUMENT NUMBER: 146:441658
TITLE: Preparation of 2-thienylurea derivatives as inhibitors of soluble epoxide hydrolase
INVENTOR(S): Takahashi, Hitomi; Ota, Tomomi; Kakinuma, Hiroyuki
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 41pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007043652	A1	20070419	WO 2006-JP320466	20061013
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: JP 2005-299465 A 20051013
OTHER SOURCE(S): MARPAT 146:441658
GI

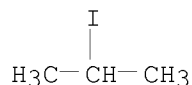


AB The title compds. I [R₁ = alkyl, cycloalkyl, etc.; R₂ = H, halo, alkyl; R₃, R₄ = H, halo, alkyl, alkoxy, etc.] are prepared I are useful in the treatment of hypertension, etc. Thus, 1-[3-chloro-4-(isopropylsulfonyl)-2-thienyl]-3-[3-(trifluoromethyl)phenyl]urea was prepared in several steps from 3-amino-4-(isopropylsulfonyl)thiophene-2-carboxylic acid Et ester. Compds. of this invention showed IC₅₀ values of 0.03 μM to 0.31 μM against soluble epoxide hydrolase.

IT 75-30-9, 2-Iodopropane
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-thienylurea derivs. as inhibitors of soluble epoxide hydrolase)

RN 75-30-9 CAPLUS

CN Propane, 2-iodo- (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

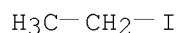
ACCESSION NUMBER: 1996:465674 CAPLUS
 DOCUMENT NUMBER: 125:161867
 ORIGINAL REFERENCE NO.: 125:30167a,30170a
 TITLE: Regioselectivity of Rhodococcus NCIMB 11216
 epoxide hydrolase: applicability of
 E-values for description of enantioselectivity depends
 on substrate structure
 AUTHOR(S): Mischitz, M.; Mirtl, C.; Saf, R.; Faber, K.
 CORPORATE SOURCE: Inst. of Organic Chemistry, Graz Univ. of Technology,
 Graz, A-8010, Austria
 SOURCE: Tetrahedron: Asymmetry (1996), 7(7), 2041-2046
 CODEN: TASYE3; ISSN: 0957-4166
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 125:161867

AB The regioselectivity of purified epoxide hydrolase
 from Rhodococcus NCIMB 11216 was investigated by hydrolyzing a series of
 structurally different epoxides 1a-5a in 18O-labeled water followed by
 GC/MS anal. of the 1,2-diols formed 1b-5b. The enzyme introduced a single
 18O-atom in a trans-specific fashion with a varying degree of
 regioselectivity depending on the substitution pattern of the substrate.
 With an aliphatic mono-1a and 2,2-disubstituted oxirane 3a the attack
 occurred exclusively at the less hindered C-atom and complete retention of
 configuration was retained. The regioselectivity was low with a 2,3-di-4a
 and a trisubstituted epoxide 5a, and with a substrate bearing a benzylic
 oxirane atom 2a. As a consequence, the 'Enantiomeric Ratio' (E) can be
 applied to describe the selectivity of kinetic resolsns. for some, but not
 for all types of substrates.

IT 75-03-6, Ethyl iodide
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reactant for preparation of epoxide hydrolase
 substrates and products)

RN 75-03-6 CAPLUS

CN Ethane, iodo- (CA INDEX NAME)



L9 ANSWER 9 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2008:1015927 CAPLUS
 TITLE: Epoxide Hydrolase Lsd19 for
 Polyether Formation in the Biosynthesis of Lasalocid
 A: Direct Experimental Evidence on Polyene-Polyepoxide
 Hypothesis in Polyether Biosynthesis
 AUTHOR(S): Shichijo, Yoshihiro; Migita, Akira; Oguri, Hiroki;
 Watanabe, Mami; Tokiwano, Tetsuo; Watanabe, Kenji;
 Oikawa, Hideaki
 CORPORATE SOURCE: Division of Chemistry, Graduate School of Science,
 Hokkaido University, Sapporo, 060-0810, Japan

SOURCE: Journal of the American Chemical Society ACS ASAP
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Polyether metabolites are an important class of natural products. Although their biosynthesis, especially construction of polyether skeletons, attracted organic chemists for many years, no exptl. data on the enzymic polyether formation has been obtained. In this study, a putative epoxide hydrolase gene lsd19 found on the biosynthetic gene cluster of an ionophore polyether lasalocid was cloned and successfully overexpressed in Escherichia coli. Using the purified Lsd19, a proposed substrate, bisepoxyprelasalocid, and its synthesized analog were successfully converted into lasalocid A and its derivative via a 6-endo-tet cyclization mode. On the other hand, treatment of the bisepoxide with trichloroacetic acid gave isolasalocid A via a 5-exo-tet cyclization mode. Therefore, the enzymic conversion observed in this study unambiguously showed that the bisepoxyprelasalocid is an intermediate of the lasalocid biosynthesis and that Lsd19 catalyzes the sequential cyclic ether formations involving an energetically disfavored 6-endo-tet cyclization. This is the first example of the enzymic epoxide-opening reactions leading to a polyether natural product.

IT INDEXING IN PROGRESS

IT 100-39-0, Benzyl bromide

RL: RCT (Reactant); RACT (Reactant or reagent)
(epoxide hydrolase Lsd19 for polyether formation in biosynthesis of lasalocid A)

RN 100-39-0 CAPLUS

CN Benzene, (bromomethyl)- (CA INDEX NAME)

Ph-CH₂-Br

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 10 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2008:370383 CAPLUS

DOCUMENT NUMBER: 148:489431

TITLE: Development of Metabolically Stable Inhibitors of Mammalian Microsomal Epoxide Hydrolase

AUTHOR(S): Morisseau, Christophe; Newman, John W.; Wheelock, Craig E.; Hill, Thomas, III; Morin, Dexter; Buckpitt, Alan R.; Hammock, Bruce D.

CORPORATE SOURCE: Department of Entomology, U. C. Cancer Center, University of California, Davis, CA, 95616, USA

SOURCE: Chemical Research in Toxicology (2008), 21(4), 951-957
CODEN: CRTOEC; ISSN: 0893-228X

PUBLISHER: American Chemical Society

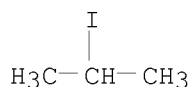
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The microsomal epoxide hydrolase (mEH) plays a significant role in the metabolism of xenobiotics such as polyarom. toxicants. Addnl., polymorphism studies have underlined a potential role of this enzyme in relation to a number of diseases, such as emphysema, spontaneous abortion, eclampsia, and several forms of cancer. We recently demonstrated that fatty amides, such as elaidamide, represent a new class of potent inhibitors of mEH. While these compds. are very active on recombinant mEH in vitro, they are quickly inactivated in liver exts.

reducing their value in vivo. We investigated the effect of structural changes on mEH inhibition potency and microsomal stability. Results obtained indicate that the presence of a small alkyl group α to the terminal amide function and a thio-ether β to this function increased mEH inhibition by an order of magnitude while significantly reducing microsomal inactivation. The addition of a hydroxyl group 9-10 carbons from the terminal amide function resulted in better inhibition potency without improving microsomal stability. The best compound obtained, 2-nonylsulfanyl-propionamide, is a competitive inhibitor of mEH with a KI of 72 nM. Furthermore, this new inhibitor significantly reduces mEH diol production in ex vivo lungs exposed to naphthalene, underlying the usefulness of the inhibitors described herein. These novel inhibitors could be valuable tools to investigate the physiol. and biol. roles of mEH.

IT 75-30-9, 2-Iodopropane
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (development of metabolically stable inhibitors of mammalian microsomal epoxide hydrolase)
 RN 75-30-9 CAPLUS
 CN Propane, 2-iodo- (CA INDEX NAME)



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 11 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:525804 CAPLUS

DOCUMENT NUMBER: 147:157043

TITLE: The role of pharmacogenetics in the metabolism of antiepileptic drugs: pharmacokinetic and therapeutic implications

AUTHOR(S): Klotz, Ulrich

CORPORATE SOURCE: Dr Margarete Fischer-Bosch Institut fuer Klinische Pharmakologie, Stuttgart, Germany

SOURCE: Clinical Pharmacokinetics (2007), 46(4), 271-279
 CODEN: CPKNDH; ISSN: 0312-5963

PUBLISHER: Wolters Kluwer Health

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. Several different factors, including pharmacogenetics, contribute to inter-individual variability in drug response. Like most other agents, many antiepileptic drugs (AEDs) are metabolized by a variety of enzymic reactions, and the cytochrome P 450 (CYP) superfamily has attracted considerable attention. Some of those CYPs exist in the form of genetic (allelic) variants, which may also affect the plasma concns. or drug exposure (area under the plasma concentration-time curve [AUC]) of AEDs. With regard to the metabolism of AEDs, the polymorphic CYP2C9 and CYP2C19 are of interest. This review summarizes the evidence as to whether such polymorphisms affect the clin. action of AEDs. In the case of mephenytoin, defects in its metabolism may be attributable to >10 mutated alleles (designated as *2, *3 and others) of the gene expressing CYP2C19. Consequently, poor metabolizers (PMs) and extensive metabolizers (EMs) could be differentiated, whose frequencies vary among ethnic populations. CYP2C19 contributes to the metabolism of diazepam and phenytoin, the latter drug also representing a substrate of CYP2C9, with its predominant variants being defined as *2 and *3. For both AEDs, there is maximally a 2-fold difference in the hepatic elimination rate (e.g. clearance) or the

AUC between the extremes of EMs and PMs which, in the case of phenytoin (an AED with a narrow 'therapeutic window'), would suggest a dosage reduction only for patients who are carriers of mutated alleles of both CYP2C19 and CYP2C9, a subgroup that is very rare among Caucasians (about 1% of the population) but more frequent in Asians (about 10%). The minor contribution of CYP2C19 to the metabolism of phenobarbital (phenobarbitone) can be overlooked. In rare cases, valproic acid can be metabolized to the reactive (hepatotoxic) metabolite, 4-ene-valproic acid. It is not yet clear whether genetic variants of the involved enzyme (CYP2C9) are responsible for this problem. Likewise, the active metabolite of carbamazepine, carbamazepine-10,11-epoxide, is transformed by the microsomal epoxide hydrolase, an enzyme that is also highly polymorphic, but the pharmacokinetic and clin. consequences still need to be evaluated. Pharmacogenetic investigations have increased our general knowledge of drug disposition and action. As for old and especially

new

AEDs the pharmacogenetic influence on their metabolism is not very striking, it is not surprising that there are no treatment guidelines taking pharmacogenetic data into account. Therefore, the traditional and validated therapeutic drug monitoring approach, representing a direct 'phenotype' assessment, still remains the method of choice when an individualized dosing regimen is anticipated. Nevertheless, pharmacogenetics and pharmacogenomics can offer some novel contributions when attempts are made to maximize drug efficacy and enhance drug safety.

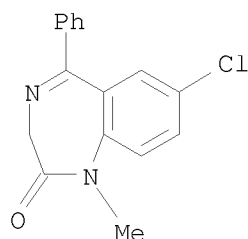
IT 439-14-5, Diazepam

RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(CYP2C9 gene influenced metabolism of diazepam in epileptic patient)

RN 439-14-5 CAPLUS

CN 2H-1,4-Benzodiazepin-2-one, 7-chloro-1,3-dihydro-1-methyl-5-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 12 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:393072 CAPLUS

DOCUMENT NUMBER: 137:216786

TITLE: Asymmetric total synthesis of (+)-exo-brevicomine based on enantioconvergent biocatalytic hydrolysis of an alkene-functionalized 2,3-disubstituted epoxide

AUTHOR(S): Mayer, Sandra F.; Mang, Harald; Steinreiber, Andreas; Saf, Robert; Faber, Kurt

CORPORATE SOURCE: Department of Chemistry, Organic & Bioorganic Chemistry, University of Graz, Graz, A-8010, Austria

SOURCE: Canadian Journal of Chemistry (2002), 80(4), 362-369
CODEN: CJCHAG; ISSN: 0008-4042

PUBLISHER: National Research Council of Canada

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 137:216786

AB A short total asym. synthesis of (+)-exo- and (-)-endo-brevicommin, which are components of the attracting pheromone system of several bark-beetle species belonging to the genera *Dendroctonus* and *Dryocoetes*, was accomplished via a chemoenzymic protocol. The key step consisted of biocatalytic hydrolysis by bacterial epoxide hydrolases of cis-configured 2,3-disubstituted oxiranes bearing olefinic side chains. This reaction proceeded in an enantioconvergent fashion, by affording a single enantiomeric vic-diol from the rac-epoxide in up to 92% ee and 83% isolated yield.

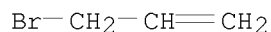
IT 106-95-6, Allyl bromide, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)

(asym. total synthesis of (+)-exo-brevicommin based on enantioconvergent biocatalytic hydrolysis of alkene-functionalized 2,3-disubstituted epoxide)

RN 106-95-6 CAPLUS

CN 1-Propene, 3-bromo- (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 13 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:326455 CAPLUS

DOCUMENT NUMBER: 131:208530

TITLE: A multi-laboratory evaluation of cryopreserved monkey hepatocyte functions for use in pharmaco-toxicology
AUTHOR(S): de Sousa, Georges; Nicolas, Florence; Placidi, Michel; Rahmani, Roger; Benicourt, Marc; Vannier, Bernard; Lorenzon, Giocondo; Mertens, Karine; Coecke, Sandra; Callaerts, Andre; Rogiers, Vera; Khan, Shamas; Roberts, Phil; Skett, Paul; Fautrel, Alain; Chesne, Christophe; Guillouzo, Andre

CORPORATE SOURCE: INSERM/Centre de Recherche Agronomique, Antibes, 06606, Fr.

SOURCE: Chemico-Biological Interactions (1999), 121(1), 77-97
CODEN: CBINA8; ISSN: 0009-2797

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Ethical, economic and tech. reasons hinder regular supply of freshly isolated hepatocytes from higher mammals such as monkey for preclin. evaluation of drugs. Hence, the authors aimed at developing optimal and reproducible protocols to cryopreserve and thaw parenchymal liver cells from this major toxicol. species. Before the routine use of these protocols, the authors validated them through a multi-laboratory study. Dissociation of the whole animal liver resulted in obtaining 1-5 billion parenchymal cells with a viability of about 86%. An appropriate fraction (around 20%) of the freshly isolated cells was immediately set in primary culture and various hepato-specific tests were performed to examine their metabolic, biochem. and toxicol. functions as well as their ultrastructural characteristics. The major part of the hepatocytes was frozen and their functionality checked using the same parameters after thawing. The characterization of fresh and thawed monkey hepatocytes demonstrated the maintenance of various hepato-specific functions. Indeed, cryopreserved hepatocytes were able to survive and to function in culture as well as their fresh counterparts. The ability for synthesis (proteins, ATP, GSH) and conjugation and secretion of biliary acids was

preserved after deep freeze storage. A better stability of drug metabolizing activities than in rodent hepatocytes was observed in monkey. After thawing, Phase I and Phase II activities (cytochrome P 450, ethoxycoumarin-O-deethylase, aldrin epoxidase, epoxide hydrolase, glutathione transferase, glutathione reductase and glutathione peroxidase) were well preserved. The metabolic patterns of several drugs were qual. and quant. similar before and after cryopreservation. Lastly, cytotoxicity tests suggested that the freezing/thawing steps did not change cell sensitivity to toxic compds.

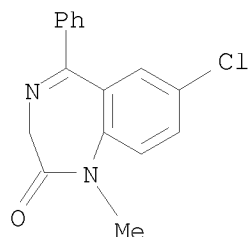
IT 439-14-5, Diazepam

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(metabolism; multi-laboratory evaluation of cryopreserved monkey hepatocyte functions for use in pharmaco-toxicol. in relation to drug metabolism)

RN 439-14-5 CAPLUS

CN 2H-1,4-Benzodiazepin-2-one, 7-chloro-1,3-dihydro-1-methyl-5-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 14 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1997:415295 CAPLUS

DOCUMENT NUMBER: 127:130797

ORIGINAL REFERENCE NO.: 127:25089a,25092a

TITLE: In vivo induction and in vitro inhibition of hepatic cytochrome P450 activity by the benzodiazepine anticonvulsants clonazepam and diazepam

AUTHOR(S): Nims, Raymond W.; Prough, Russell A.; Jones, Collins R.; Stockus, Diana L.; Dragnev, Konstantin H.; Thomas, Paul E.; Lubet, Ronald A.

CORPORATE SOURCE: Chemistry Section, Laboratory of Comparative Carcinogenesis and Biological Carcinogenesis and Development Program, National Cancer Inst., USA

SOURCE: Drug Metabolism and Disposition (1997), 25(6), 750-756
CODEN: DMDSAI; ISSN: 0090-9556

PUBLISHER: Williams & Wilkins

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The ability of the benzodiazepines, as a chemical class, to cause the induction and/or inhibition of cytochromes P 450 has not been well characterized. In the present study, the induction of the cytochrome P 450 2B subfamily (CYP2B) in vivo and the inhibition of CYP2B activity in vitro by selected benzodiazepines was examined in hepatic tissues derived from male F344/NCr rats. Initial studies of the in vivo induction or in vitro inhibition of benzyloxyresorufin O-dealkylation activity revealed that both clonazepam and diazepam were relatively effective in vivo inducers of CYP2B when administered in the diet at 500 ppm for 5 days and also were fairly potent inhibitors of the activity of these hemoproteins in vitro. Oxazepam, in contrast, was ineffective as an inducer or an

inhibitor of this activity. Further studies were performed to characterize the subfamily selectivity of the P 450 induction and inhibition displayed by clonazepam. Specifically, microsomes from rats treated with clonazepam (1000 or 1800 ppm in the diet for 5 days) were found to be highly induced with respect to catalytic activities mediated by CYP2B, including benzyloxyresorufin and pentoxyresorufin O-dealkylation or testosterone 16 β -hydroxylation, but other CYP proteins were minimally induced. In addition to inducing the CYP2B subfamily, clonazepam also induced the RNA encoding other drug metabolizing enzymes (e.g., epoxide hydrolase and the glutathione S-transferase α -subfamily) that are typically induced by phenobarbital-type inducers. Finally, clonazepam proved to be a potent noncompetitive or "mixed-type" competitive inhibitor of catalytic activities mediated by CYP2B, but not by other CYP proteins (e.g. CYP2A, CYP3A) in microsomes derived from phenobarbital-pretreated rats.

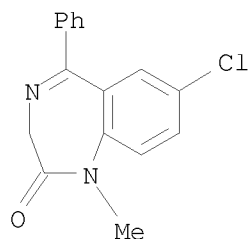
IT 439-14-5, Diazepam

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(benzodiazepine anticonvulsants induction and inhibition of hepatic cytochrome P 450 activity)

RN 439-14-5 CAPLUS

CN 2H-1,4-Benzodiazepin-2-one, 7-chloro-1,3-dihydro-1-methyl-5-phenyl- (CA INDEX NAME)



L9 ANSWER 15 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:407002 CAPLUS

Correction of: 2005:155217

DOCUMENT NUMBER: 143:248210

Correction of: 142:240243

TITLE: Product class 2: pyridinones and related systems

AUTHOR(S): Keller, P. A.

CORPORATE SOURCE: Germany

SOURCE: Science of Synthesis (2005), 15, 285-387

CODEN: SSCYJ9

PUBLISHER: Georg Thieme Verlag

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

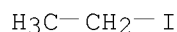
AB A review of methods to prepare pyridinones and related systems is presented. Synthetic methods include cyclization, aromatization, ring transformation, and substituent modification. The parent pyridinones are generally stable and are easily handled under standard laboratory conditions. The corresponding pyridinethiones are generally more reactive but have the advantage of generally requiring only standard laboratory equipment for their handling. The pyridineselenones are more reactive and the pyridinetellurones have not been comprehensively studied and characterized due to their reactivity and associated difficulty in production

IT 75-03-6 106-95-6, reactions

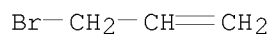
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of pyridinones and related derivs. via cyclization,

aromatization, ring transformation, and substituent modification)
RN 75-03-6 CAPLUS
CN Ethane, iodo- (CA INDEX NAME)



RN 106-95-6 CAPLUS
CN 1-Propene, 3-bromo- (CA INDEX NAME)



L9 ANSWER 16 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:767853 CAPLUS

DOCUMENT NUMBER: 141:410476

TITLE: Polystyrene-supported α -seleno carbanions:
Efficient reagents for highly stereocontrolled
syntheses of vinylphosphonates and vinyl sulfones

AUTHOR(S): Xu, Wei Ming; Tang, E.; Huang, Xian

CORPORATE SOURCE: Department of Chemistry, Zhejiang University,
Hangzhou, 310028, Peop. Rep. China

SOURCE: Synthesis (2004), (13), 2094-2098

CODEN: SYNTBF; ISSN: 0039-7881

PUBLISHER: Georg Thieme Verlag

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 141:410476

AB Polystyrene-supported selenomethylphosphonate and polystyrene-supported
selenomethyl sulfones have been prepared These novel reagents were treated
with LDA or BuLi to produce polystyrene-supported α -seleno
carbanions, which reacted with alkyl halides, followed by stereospecific
selenoxide syn-elimination to give E-vinylphosphonates and E-vinyl
sulfones resp. Also these novel polymer reagents can be regenerated and
reused.

IT 100-39-0, Benzyl bromide 106-95-6, Allyl bromide,
reactions

RL: RCT (Reactant); RACT (Reactant or reagent)

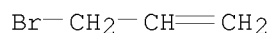
(stereocontrolled synthesis of vinylphosphonates and vinyl sulfones
using polystyrene-supported selenomethylphosphonate and selenomethyl
sulfone)

RN 100-39-0 CAPLUS

CN Benzene, (bromomethyl)- (CA INDEX NAME)



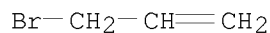
RN 106-95-6 CAPLUS
CN 1-Propene, 3-bromo- (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 17 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1977:189112 CAPLUS
DOCUMENT NUMBER: 86:189112
ORIGINAL REFERENCE NO.: 86:29653a,29656a
TITLE: The unsaturated esters of diselenophosphoric acid
AUTHOR(S): Zemlyanskii, N. L.; Mel'nik, Ya. G.; Turkevich, V. V.;
Makota, I. P.; Koretskii, A. S.
CORPORATE SOURCE: USSR
SOURCE: Visnik L'vivs'kogo Derzhavnogo Universitetu, Seriya
Khimichna (1975), 17, 65-8
CODEN: VLDUAB; ISSN: 0460-0509
DOCUMENT TYPE: Journal
LANGUAGE: Ukrainian
AB (RO)2P(Se)SeH (R = Et, Pr, Me2CH, Bu) were neutralized with
K2CO3 and then treated with R1Br (R1 = allyl, HC.tplbond.CCH2) in Me2CO at
40° to give 71-82% (RO)2P(Se)SeR1 (I). Mol. association was deduced
from the IR spectra of all 4 I (R1 = CH2C.tplbond.CH).
IT 106-95-6, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of dialkyl diselenophosphates with)
RN 106-95-6 CAPLUS
CN 1-Propene, 3-bromo- (CA INDEX NAME)



L9 ANSWER 18 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1994:455036 CAPLUS
DOCUMENT NUMBER: 121:55036
ORIGINAL REFERENCE NO.: 121:9891a
TITLE: Enhanced blood pressure response to mineralocorticoid
stimulation in normotensive members of hypertensive
families
AUTHOR(S): Ferrari, Paolo; Travaglini, Marco; Schild, Christoph;
Allemann, Yves; Shaw, Sidney; Weidmann, Peter
CORPORATE SOURCE: Med. Poliklin., Univ. Berne, Switz.
SOURCE: Blood Pressure (1992), 1(2), 86-91
CODEN: BLPREG; ISSN: 0803-7051
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Currently normotensive offspring of essential hypertensive parents often
have disturbances in blood pressure (BP) regulation such as abnormalities
in electrolyte homeostasis, increased salt-sensitivity and/or impaired
renal Na+-excretion. Whether an altered reactivity to mineralocorticoids
may also play a role is presently unknown. Therefore, the authors
investigated BP (recorded during 24 h), plasma atrial natriuretic factor
(ANF), cyclic guanosine monophosphate (cGMP), aldosterone (PA) and renin
activity (PRA), 24-h urine electrolyte and cGMP excretions measured on 4
consecutive days, as well as other variables, after 1 wk on placebo and
after 3 wk of 9 α -fludrocortisoneacetate (9 α F) administration,
0.6 mg/d in 12 normotensive sons of essential hypertensive parents (SEH)
and 12 body-mass-index- and age-matched (25 \pm 1[\pm SEM]yr) sons of normotensive
parents (SN). On placebo, the 2 groups did not differ significantly in
average 24 h BP (mean BP 95 \pm 2 mmHg), plasma-ANF (40 \pm 7 vs 30 \pm 5 pg/mL),
cGMP (6 \pm 0.4 vs 6 \pm 0.5 nmol/L), PRA (1.3 \pm 0.1 vs 1.6 \pm 0.2 ng/mL/h), PA (9 \pm 0.5 vs
10 \pm 0.9 ng/dL), hematocrit (44 \pm 0.7 vs 44 \pm 0.4%) and 96-h urinary-Na+ (mean
205 \pm 13 vs 195 \pm 16 mmol/d), -K+ (69 \pm 6 vs 78 \pm 7 mmol/d) or -cGMP (461 \pm 35
vs 483 \pm 32 nmol/d). 9 α F significantly increased BP in SEH

($p < 0.005$) but not SN (107 ± 2 vs 100 ± 2 mmHg, $p < 0.05$). Elevation of BP during the night accounted for this difference ($+13$ vs $+8$ mmHg, $p < 0.02$). However, during 9aF the 2 groups did not differ with regard of plasma ANF (106 ± 13 vs 100 ± 14 pg/mL), cGMP (10 ± 1.1 vs 10 ± 1.4 nmol/L), PRA (0.5 ± 0.1 vs 0.5 ± 0.2 ng/mL/h), PA (5 ± 0.3 vs 4 ± 0.3 ng/dL), 96-h urinary-Na⁺ (205 ± 19 vs 195 ± 17 mmol/d), -K⁺ (80 ± 8 vs 69 ± 6 mmol/d) or -cGMP (673 ± 76 vs 653 ± 62 nmol/d), plasma-Na⁺ (increase $+3$ vs $+2$ mmol/L), K⁺ (decrease -0.5 vs -0.5 mmol/L), hematocrit (42 ± 0.8 vs $42 \pm 0.2\%$) or body weight (increase $+2.0$ vs $+1.9$ kg). These results indicate that normotensive offspring of hypertensive parents may react to mineralocorticoid stimulation with an enhanced BP-increase. This disturbance cannot be explained by insufficient renin-aldosterone suppression, inadequate ANF stimulation or abnormally increased Na⁺-fluid retention.

IT 9015-94-5, Renin, biological studies

RL: BIOL (Biological study)

(in plasma of normotensive sons from essential hypertensive families, enhanced blood pressure response to mineralocorticoid in relation to)

RN 9015-94-5 CAPLUS

CN Renin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L9 ANSWER 19 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1938:63839 CAPLUS

DOCUMENT NUMBER: 32:63839

ORIGINAL REFERENCE NO.: 32:8937i,8938a

TITLE: Raman effect. LXXXVI. Ethyl derivatives

AUTHOR(S): Wagner, J.

SOURCE: Z. physik. Chem. (1938), B40, 439-49

DOCUMENT TYPE: Journal

LANGUAGE: Unavailable

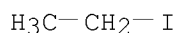
AB cf. C. A. 32, 6549.5. Raman spectra were obtained for EtX, where X = OH, SH, Cl and I. Results of other investigations, where X = Me, NH₂, Br and SeH have been included in the calcns. The mols. have been treated as a 3-particle system with a valence force potential energy function. The calculated vibrational frequencies agree with experiment only if the atomic weight of

X is less than 36. The valence force consts. are smaller and the nuclear distances are larger than those for the corresponding methyl derivs.

IT 75-03-6, Ethane, iodo-
(Raman spectrum of)

RN 75-03-6 CAPLUS

CN Ethane, iodo- (CA INDEX NAME)



L9 ANSWER 20 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1220997 CAPLUS

DOCUMENT NUMBER: 148:1283

TITLE: Estrogen receptor α is a major contributor to estrogen-mediated fetal testis dysgenesis and cryptorchidism

AUTHOR(S): Cederroth, Christopher R.; Schaad, Olivier; Descombes, Patrick; Chambon, Pierre; Vassalli, Jean-Dominique; Nef, Serge

CORPORATE SOURCE: Department of Genetic Medicine and Development, National Center of Competence in Research Frontiers in

SOURCE: Genetic, University of Geneva, Geneva, 1211/4, Switz.
Endocrinology (2007), 148(11), 5507-5519
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Failure of the testes to descend into the scrotum (cryptorchidism) is one of the most common birth defects in humans. In utero exposure to estrogens, such as 17 β -estradiol (E2) or the synthetic estrogen diethylstilbestrol (DES), down-regulates insulin-like 3 (Insl3) expression in embryonic Leydig cells, which in turn results in cryptorchidism in mice. To identify the mol. mechanism whereby xenoestrogens block Insl3 gene transcription, we performed a microarray anal. of wild-type or estrogen receptor (ER) α -mutant testes exposed in utero to pharmacol. doses of E2 or DES. Six and 31 genes were resp. down-regulated and up-regulated by estrogen exposure (≥ 4 -fold). All six genes down-regulated by estrogen exposure, including Insl3 and the steroidogenic genes steroidogenic acute regulatory protein and cytochrome P 450 17 α -hydroxylase/17,20-lyase, were done so by an ER α -dependent mechanism. In contrast, up-regulation was mediated either by ER α for 12 genes or by an independent mechanism for the 19 remaining genes. Finally, we show that Insl3 gene expression and testicular descent were not affected by in utero exposure to E2 or DES in ER α mutant mice, whereas absence of ER β did not influence the effect of these estrogens. Collectively, these data demonstrate that xenoestrogens inhibit the endocrine functions of fetal Leydig cells through an ER α -dependent mechanism.

IT 9015-94-5, Renin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(estrogen receptor α contribution to estrogen-mediated fetal testis dysgenesis and cryptorchidism)

RN 9015-94-5 CAPLUS
CN Renin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 21 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:817105 CAPLUS

DOCUMENT NUMBER: 147:182868

TITLE: Use of DNA microarrays, gene expression profiles, and computer models for predicting cardiotoxicity of substances

INVENTOR(S): Mendrick, Donna L.; Johnson, Kory R.; Daniels, Kellye K.; Porter, Mark W.

PATENT ASSIGNEE(S): Gene Logic, Inc., USA

SOURCE: PCT Int. Appl., 203pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	---	-----	-----	-----
WO 2007084187	A2	20070726	WO 2006-US33712	20060828
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,			

MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS,
 RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ,
 UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
 CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
 GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2005-711444P P 20050826

AB The present invention includes methods of predicting cardiotoxicity of test agents and methods of generating cardiotoxicity prediction models using algorithms for analyzing quant. gene expression information. The invention also includes microarrays, computer systems comprising the toxicity prediction models, as well as methods of using the computer systems by remote users for determining the toxicity of test agents.

IT 9015-94-5, Renin, biological studies
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (use of DNA microarrays, gene expression profiles, and computer models for predicting cardiotoxicity of substances)

RN 9015-94-5 CAPLUS

CN Renin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L9 ANSWER 22 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:1248277 CAPLUS

DOCUMENT NUMBER: 146:22551

TITLE: Random mutagenesis, screening and selection of protease variants with altered sensitivity to activity modulators

INVENTOR(S): Koltermann, Andre; Kettling, Ulrich; Haupts, Ulrich; Coco, Wayne; Tebbe, Jan; Votsmeier, Christian; Scheidig, Andreas

PATENT ASSIGNEE(S): Direvo Biotech AG, Germany

SOURCE: Eur. Pat. Appl., 93pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
EP 1726643	A1	20061129	EP 2005-104543	20050527
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				
US 20060269538	A1	20061130	US 2006-441635	20060526
WO 2006125827	A1	20061130	WO 2006-EP62644	20060526
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,				

KG, KZ, MD, RU, TJ, TM
 EP 1883696 A1 20080206 EP 2006-763303 20060526
 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR
 PRIORITY APPLN. INFO.: EP 2005-104543 A 20050527
 US 2005-685566P P 20050527
 US 2005-686021P P 20050531
 WO 2006-EP62644 W 20060526

AB The present invention provides a method for the selection of proteases with altered sensitivity to one or more activity-modulating substances. The method combines the provision of a protease library (i.e., phage display library) encoding polynucleotide sequences generated by using PCR mutagenesis, expression of the enzymes, screening of the library in the presence of one or several activity-modulating substances, selection of variants with altered sensitivity to one or several activity-modulating substances and isolation of those polynucleotide sequences that encode for the selected variants. In particular, mutant variants of human trypsin are disclosed.

IT 9015-94-5P, Renin, biological studies
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (random mutagenesis, screening and selection of protease variants with altered sensitivity to activity modulators)

RN 9015-94-5 CAPLUS
 CN Renin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 23 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:712565 CAPLUS

DOCUMENT NUMBER: 138:470

TITLE: Failure of normal adult Leydig cell development in androgen-receptor-deficient mice

AUTHOR(S): O'Shaughnessy, Peter J.; Johnston, Heather; Willerton, Louise; Baker, Paul J.

CORPORATE SOURCE: Institute of Comparative Medicine, University of Glasgow Veterinary School, Glasgow, G61 1QH, UK

SOURCE: Journal of Cell Science (2002), 115(17), 3491-3496
 CODEN: JNCSAI; ISSN: 0021-9533

PUBLISHER: Company of Biologists Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB During testicular development, fetal and adult populations of Leydig cells arise sequentially. Previous studies have shown that androgen action is required for normal steroidogenic activity in the mouse testis. Therefore, to determine the role of androgens in regulating fetal and adult Leydig cell differentiation and function, Leydig development has been measured in mice lacking functional androgen receptors (AR-null). The Leydig cell number was normal on day 5 after birth in AR-null mice but failed to increase normally thereafter and was about 30% of the control level on day 20 and about 60% of control level in adult animals. Levels of 15 different mRNA species expressed specifically in Leydig cells were measured by real-time PCR in AR-null and control animals. Expression levels of all mRNA species were normal on day 5 when only fetal Leydig cells are present. In older animals, which contain predominantly adult Leydig cells, five of the mRNA species (β -hydroxysteroid dehydrogenase (β HSD) type 1, cytochrome P 450scc, renin, StAR protein and luteinising hormone receptor) were expressed at normal or increased levels in AR-null mice. All other mRNA species measured showed

significantly reduced expression in older animals, and three of these mRNA species (17 β -hydroxysteroid dehydrogenase type III, prostaglandin D (PGD)-synthetase and 3 β HSD type VI), which are only expressed in the adult population of Leydig cells, were barely detectable in the adult AR-null mouse. The results show that in the absence of androgen receptors, fetal Leydig cell function is normal, but there is a developmental failure of adult Leydig cell maturation, with cells only acquiring partial characteristics of the adult population.

IT 9015-94-5, Renin, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(androgen receptor role in regulating fetal and adult Leydig cell differentiation and function in development)

RN 9015-94-5 CAPLUS

CN Renin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 24 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:929794 CAPLUS

DOCUMENT NUMBER: 137:89189

TITLE: Identification of novel peroxisome
proliferator-activated receptor α (PPAR α)
target genes in mouse liver using cDNA microarray
analysis

AUTHOR(S): Cherkaoui-Malki, Mustapha; Meyer, Kirstin; Cao,
Wen-Qing; Latruffe, Norbert; Yeldandi, Anjana V.; Rao,
M. Sambasiva; Bradfield, Christopher A.; Reddy,
Janardan K.

CORPORATE SOURCE: Department of Pathology, Northwestern University
Medical School, Chicago, IL, 60611-3008, USA

SOURCE: Gene Expression (2001), 9(6), 291-304

CODEN: GEEXEJ; ISSN: 1052-2166

PUBLISHER: Cognizant Communication Corp.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Peroxisome proliferators, which function as peroxisome
proliferator-activated receptor- α (PPAR α) agonists, are a
group of structurally diverse nongenotoxic hepatocarcinogens including the
fibrate class of hypolipidemic drugs that induce peroxisome proliferation
in liver parenchymal cells. Sustained activation of PPAR α by these
agents leads to the development of liver tumors in rats and mice. To
understand the mol. mechanisms responsible for the pleiotropic effects of
these agents, we have utilized the cDNA microarray to generate a mol.
portrait of gene expression in the liver of mice treated for 2 wk with
Wy-14,643, a potent peroxisome proliferator. PPAR α activation
resulted in the stimulation of expression (fourfold or greater) of 36
genes and decreased the expression (fourfold or more decrease) of 671
genes. Enhanced expression of several genes involved in lipid and glucose
metabolism and many other genes associated with peroxisome biogenesis, cell
surface function, transcription, cell cycle, and apoptosis has been observed
These include: CYP2B9, CYP2B10, monoglyceride lipase, pyruvate
dehydrogenase-kinase-4, cell death-inducing DNA-fragmentation
factor- α , peroxisomal biogenesis factor 11 β , as well as several
cell recognition surface proteins including annexin A2, CD24, CD39,
lymphocyte antigen 6, and retinoic acid early transcript- γ , among
others. Northern blotting of total RNA extracted from the livers of
PPAR α -/- mice and from mice lacking both PPAR α and peroxisomal
fatty acyl-CoA oxidase (AOX), that were fed control and Wy-14,643-containing
diets for 2 wk, as well as time course of induction following a single

dose of Wy-14,643, revealed that upregulation of genes identified by microarray procedure is dependent upon peroxisome proliferation vis-a-vis PPAR α . However, cell death-inducing DNA-fragmentation factor- α mRNA, which is increased in the livers of wild-type mice treated with peroxisome proliferators, was not enhanced in AOX-/- mice with spontaneous peroxisome proliferation. These observations indicate that the activation of PPAR α leads to increased and decreased expression of many genes not associated with peroxisomes, and that delayed onset of enhanced expression of some genes may be the result of metabolic events occurring secondary to PPAR α activation and alterations in lipid metabolism

IT 9015-94-5, Renin, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (identification of peroxisome proliferator-activated receptor α
 (PPAR α) target genes in mouse liver using cDNA microarray anal.)
 RN 9015-94-5 CAPLUS
 CN Renin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 25 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:338762 CAPLUS

DOCUMENT NUMBER: 134:362292

TITLE: Methods of determining individual hypersensitivity to
 a pharmaceutical agent from gene expression profile

INVENTOR(S): Farr, Spencer

PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA

SOURCE: PCT Int. Appl., 222 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103
WO 2001032928	A3	20020725		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 1999-165398P P 19991105
 US 2000-196571P P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to determine the hypersensitivity of individuals to a given agent, such as drug or other chemical, in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes associated with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes associated with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal

individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes associated with hypersensitivity. The expression of the genes predetd. to be associated with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and apparatus useful for identifying hypersensitivity in a subject are also disclosed.

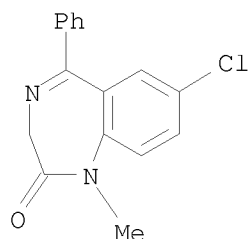
IT 439-14-5, Diazepam

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile)

RN 439-14-5 CAPLUS

CN 2H-1,4-Benzodiazepin-2-one, 7-chloro-1,3-dihydro-1-methyl-5-phenyl- (CA INDEX NAME)



L9 ANSWER 26 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2008:991947 CAPLUS

DOCUMENT NUMBER: 149:245463

TITLE: Sodium Hydrogen Selenide

AUTHOR(S): Mlochowski, Jacek; Syper, Ludwik

CORPORATE SOURCE: Pol.

SOURCE: e-EROS Encyclopedia of Reagents for Organic Synthesis (2001), No pp. given. John Wiley & Sons, Inc.: Hoboken, N. J.

CODEN: 69KUHI

URL: <http://www3.interscience.wiley.com/cgi-bin/mrwhome/104554785/HOME>

DOCUMENT TYPE: Conference; General Review; (online computer file)

LANGUAGE: English

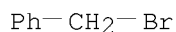
AB A review of the article Sodium Hydrogen Selenide.

IT 100-39-0

RL: RCT (Reactant); RACT (Reactant or reagent)
(Sodium Hydrogen Selenide)

RN 100-39-0 CAPLUS

CN Benzene, (bromomethyl)- (CA INDEX NAME)



L9 ANSWER 27 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:358279 CAPLUS

Correction of: 2005:481371

DOCUMENT NUMBER: 145:123921

Correction of: 143:26021

TITLE: Acyclic and cyclic carbonic acids and esters, and their sulfur, selenium, and tellurium analogues

AUTHOR(S): Jung, K. W.; Nagle, A. S.

CORPORATE SOURCE: Dept. of Chemistry, University of South Florida, Tampa, FL, 33620-5250, USA

SOURCE: Science of Synthesis (2005), 18, 379-450
CODEN: SSCYJ9

PUBLISHER: Georg Thieme Verlag

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review of the preparation and synthetic applications of acyclic and cyclic carbonic acids and esters, and their sulfur, selenium, and tellurium analogs.

IT 100-39-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and synthetic applications of acyclic and cyclic carbonic acids and esters, and their sulfur, selenium, and tellurium analogs)

RN 100-39-0 CAPLUS

CN Benzene, (bromomethyl)- (CA INDEX NAME)

Ph-CH₂-Br

L9 ANSWER 28 OF 28 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:495306 CAPLUS

DOCUMENT NUMBER: 144:128468

TITLE: Solid-phase synthesis of vinyl sulfones using polystyrene-supported selenomethyl phenyl sulfone

AUTHOR(S): Sheng, Shou Ri; Zhou, Wei; Liu, Xiao Ling; Xin, Qin; Song, Cai Sheng

CORPORATE SOURCE: Institutes of Chemistry, Jiangxi Normal University, Nanchang, 330027, Peop. Rep. China

SOURCE: Chinese Chemical Letters (2005), 16(5), 583-584
CODEN: CCLEE7; ISSN: 1001-8417

PUBLISHER: Chinese Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 144:128468

AB The solid-phase preparation of vinyl sulfones via a novel polystyrene-supported selenomethyl Ph sulfone reagent was reported.

IT 100-39-0, Benzyl bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of vinyl sulfones by solid-phase reaction of chloromethylphenylsulfone with primary alkyl halides using polystyrene-supported selenium reagent)

RN 100-39-0 CAPLUS

CN Benzene, (bromomethyl)- (CA INDEX NAME)

Ph-CH₂-Br

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L8 ANSWER 1 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2008:1015927 CAPLUS
TITLE: Epoxide Hydrolase Lsd19 for
Polyether Formation in the Biosynthesis of Lasalocid
A: Direct Experimental Evidence on Polyene-Polyepoxide
Hypothesis in Polyether Biosynthesis
AUTHOR(S): Shichiho, Yoshihiro; Migita, Akira; Oguri, Hiroki;
Watanabe, Mami; Tokiwano, Tetsuo; Watanabe, Kenji;
Oikawa, Hideaki
CORPORATE SOURCE: Division of Chemistry, Graduate School of Science,
Hokkaido University, Sapporo, 060-0810, Japan
SOURCE: Journal of the American Chemical Society ACS ASAP
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Polyether metabolites are an important class of natural products.
Although their biosynthesis, especially construction of polyether skeletons,
attracted organic chemists for many years, no exptl. data on the enzymic
polyether formation has been obtained. In this study, a putative
epoxide hydrolase gene lsd19 found on the biosynthetic
gene cluster of an ionophore polyether lasalocid was cloned and
successfully overexpressed in Escherichia coli. Using the purified Lsd19,
a proposed substrate, bisepoxytelasalocid, and its synthesized analog
were successfully converted into lasalocid A and its derivative via a
6-endo-tet cyclization mode. On the other hand, treatment of the
bisepoxide with trichloroacetic acid gave isolasalocid A via a 5-exo-tet
cyclization mode. Therefore, the enzymic conversion observed in this study
unambiguously showed that the bisepoxytelasalocid is an intermediate of
the lasalocid biosynthesis and that Lsd19 catalyzes the sequential cyclic
ether formations involving an energetically disfavored 6-endo-tet
cyclization. This is the first example of the enzymic epoxide-opening
reactions leading to a polyether natural product.

IT INDEXING IN PROGRESS

IT 100-39-0, Benzyl bromide

RL: RCT (Reactant); RACT (Reactant or reagent)

(epoxide hydrolase Lsd19 for polyether formation in
biosynthesis of lasalocid A)

RN 100-39-0 CAPLUS

CN Benzene, (bromomethyl)- (CA INDEX NAME)

Ph-CH₂-Br

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2008:991947 CAPLUS
DOCUMENT NUMBER: 149:245463
TITLE: Sodium Hydrogen Selenide
AUTHOR(S): Mlochowski, Jacek; Syper, Ludwik
CORPORATE SOURCE: Pol.
SOURCE: e-EROS Encyclopedia of Reagents for Organic Synthesis
(2001), No pp. given. John Wiley & Sons, Inc.:
Hoboken, N. J.
CODEN: 69KUHI
URL: <http://www3.interscience.wiley.com/cgi-bin/mrwhome/104554785/HOME>
DOCUMENT TYPE: Conference; General Review; (online computer file)

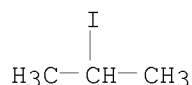
LANGUAGE: English
AB A review of the article Sodium Hydrogen Selenide.
IT 100-39-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(Sodium Hydrogen Selenide)
RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)

Ph-CH₂-Br

L8 ANSWER 3 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2008:370383 CAPLUS
DOCUMENT NUMBER: 148:489431
TITLE: Development of Metabolically Stable Inhibitors of
Mammalian Microsomal Epoxide
Hydrolase
AUTHOR(S): Morisseau, Christophe; Newman, John W.; Wheelock,
Craig E.; Hill, Thomas, III; Morin, Dexter; Buckpitt,
Alan R.; Hammock, Bruce D.
CORPORATE SOURCE: Department of Entomology, U. C. Cancer Center,
University of California, Davis, CA, 95616, USA
SOURCE: Chemical Research in Toxicology (2008), 21(4), 951-957
CODEN: CRTOEC; ISSN: 0893-228X
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The microsomal epoxide hydrolase (mEH) plays a
significant role in the metabolism of xenobiotics such as polyarom. toxicants.
Addnl., polymorphism studies have underlined a potential role of this
enzyme in relation to a number of diseases, such as emphysema, spontaneous
abortion, eclampsia, and several forms of cancer. We recently
demonstrated that fatty amides, such as elaidamide, represent a new class
of potent inhibitors of mEH. While these compds. are very active on
recombinant mEH in vitro, they are quickly inactivated in liver exts.
reducing their value in vivo. We investigated the effect of structural
changes on mEH inhibition potency and microsomal stability. Results
obtained indicate that the presence of a small alkyl group α to the
terminal amide function and a thio-ether β to this function increased
mEH inhibition by an order of magnitude while significantly reducing
microsomal inactivation. The addition of a hydroxyl group 9-10 carbons from
the terminal amide function resulted in better inhibition potency without
improving microsomal stability. The best compound obtained,
2-nonylsulfanyl-propionamide, is a competitive inhibitor of mEH with a KI
of 72 nM. Furthermore, this new inhibitor significantly reduces mEH diol
production in ex vivo lungs exposed to naphthalene, underlying the usefulness
of the inhibitors described herein. These novel inhibitors could be
valuable tools to investigate the physiol. and biol. roles of mEH.

IT 75-30-9, 2-Iodopropane
RL: RCT (Reactant); RACT (Reactant or reagent)
(development of metabolically stable inhibitors of mammalian microsomal
epoxide hydrolase)
RN 75-30-9 CAPLUS
CN Propane, 2-iodo- (CA INDEX NAME)



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1220997 CAPLUS

DOCUMENT NUMBER: 148:1283

TITLE: Estrogen receptor α is a major contributor to estrogen-mediated fetal testis dysgenesis and cryptorchidism

AUTHOR(S): Cederroth, Christopher R.; Schaad, Olivier; Descombes, Patrick; Chambon, Pierre; Vassalli, Jean-Dominique; Nef, Serge

CORPORATE SOURCE: Department of Genetic Medicine and Development, National Center of Competence in Research Frontiers in Genetic, University of Geneva, Geneva, 1211/4, Switz.

SOURCE: Endocrinology (2007), 148(11), 5507-5519

CODEN: ENDOAO; ISSN: 0013-7227

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Failure of the testes to descend into the scrotum (cryptorchidism) is one of the most common birth defects in humans. In utero exposure to estrogens, such as 17 β -estradiol (E2) or the synthetic estrogen diethylstilbestrol (DES), down-regulates insulin-like 3 (Insl3) expression in embryonic Leydig cells, which in turn results in cryptorchidism in mice. To identify the mol. mechanism whereby xenoestrogens block Insl3 gene transcription, we performed a microarray anal. of wild-type or estrogen receptor (ER) α -mutant testes exposed in utero to pharmacol. doses of E2 or DES. Six and 31 genes were resp. down-regulated and up-regulated by estrogen exposure (≥ 4 -fold). All six genes down-regulated by estrogen exposure, including Insl3 and the steroidogenic genes steroidogenic acute regulatory protein and cytochrome P 450 17 α -hydroxylase/17,20-lyase, were done so by an ER α -dependent mechanism. In contrast, up-regulation was mediated either by ER α for 12 genes or by an independent mechanism for the 19 remaining genes. Finally, we show that Insl3 gene expression and testicular descent were not affected by in utero exposure to E2 or DES in ER α mutant mice, whereas absence of ER β did not influence the effect of these estrogens. Collectively, these data demonstrate that xenoestrogens inhibit the endocrine functions of fetal Leydig cells through an ER α -dependent mechanism.

IT 9015-94-5, Renin, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(estrogen receptor α contribution to estrogen-mediated fetal testis dysgenesis and cryptorchidism)

RN 9015-94-5 CAPLUS

CN Renin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 5 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1061416 CAPLUS

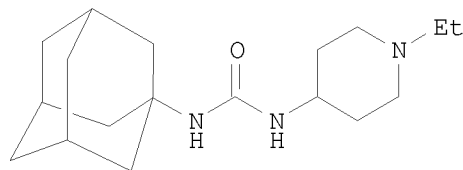
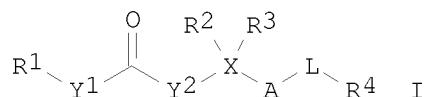
DOCUMENT NUMBER: 147:385844

TITLE: Preparation of heterocyclic urea derivatives particularly piperidinyl ureas as inhibitors of soluble epoxide hydrolase for the treatment of hypertension, inflammation and other diseases

INVENTOR(S): Hammock, Bruce D.; Jones, Paul D.; Morisseau,

Christophe; Huang, Huazhang; Tsai, Hsing-Ju; Gless, Richard, Jr.
PATENT ASSIGNEE(S): The Regents of the University of California, USA;
Arete Therapeutics
SOURCE: PCT Int. Appl., 116pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007106525	A1	20070920	WO 2007-US6412	20070313
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 20070225283	A1	20070927	US 2007-685674	20070313
PRIORITY APPLN. INFO.:			US 2006-782172P	P 20060313
OTHER SOURCE(S):			MARPAT 147:385844	
GI				



II

AB Title compds. I [R1 = (un)substituted alkyl, arylalkyl, cycloalkyl or heterocyclyl; Y1 = bond, C(R5)2, NR5 or O; Y2 = bond, NR5 and O; X = (CH2)n, wherein n = 0-1; R2, R3 and R5 independently = H, alkyl or COR6, wherein R6 = H, OH, NH2, alkyl or alkoxy; R4 = H, (un)substituted (hetero)alkyl, alkenyl, alkynyl, arylalkyl, cycloalkyl or heterocyclyl; A = (un)substituted heterocyclyl; L = direct bond, (hetero)alkylene, cycloalkylene, (hetero)arylene, CO, Se or SOm, wherein m = 0-2], and their pharmaceutically acceptable salts, are prepared and disclosed as inhibitors of soluble epoxide hydrolase (sEH). Thus, e.g., II was prepared by the reaction of 4-aminopiperidine with benzaldehyde and further protection with BOC-anhydride to provide intermediate carbamate which underwent acylation with 1-adamantyl isocyanate followed by deprotection and alkylation with bromoethane. I have an IC50 value against sEH of ≤ 150 nM. As inhibitors of sEH,

I should prove useful for the treatment of hypertension, inflammation, adult respiratory distress syndrome, diabetic complications, end stage renal disease, Raynaud syndrome and arthritis. The invention also disclosed a cis-epoxyeicosantrienoic acid (EET) which can be administered with the sEH inhibitor (no data).

IT 100-39-0, Benzylbromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of heterocyclic urea derivs. particularly piperidinyl ureas as inhibitors of soluble epoxide hydrolase for the treatment of hypertension, inflammation and other diseases)
RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)

Ph-CH₂-Br

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 6 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:1048489 CAPLUS

DOCUMENT NUMBER: 147:517065

TITLE: Stereochemical preference of yeast epoxide hydrolase for the O-axial C3 epimers of 1-oxaspiro[2.5]octanes

AUTHOR(S): Weijers, Carel A. G. M.; Koenst, Paul M.; Franssen, Maurice C. R.; Sudhoelter, Ernst J. R.

CORPORATE SOURCE: Laboratory of Organic Chemistry, Wageningen University, Wageningen, 6703HB, Neth.

SOURCE: Organic & Biomolecular Chemistry (2007), 5(19), 3106-3114

CODEN: OBCRAK; ISSN: 1477-0520

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

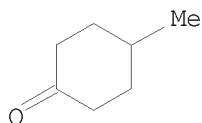
OTHER SOURCE(S): CASREACT 147:517065

AB The 1-oxaspiro[2.5]octane moiety is a common motif in many biol. active spiroepoxide compds. Stereochem. plays an important role in the action of these spiroepoxides, since the O-axial C3 epimers are predominantly responsible for biol. activity. In view of this, the reactivity of the yeast epoxide hydrolase (YEH) from *Rhodotorula glutinis* towards both O-axial and O-equatorial C3 epimers of various 1-oxaspiro[2.5]octanes was investigated. O-axial C3 Epimers were hydrolyzed faster than the O-equatorial C3 epimers. The stereochem. preference was greatly dependent on the type of substitution on the cyclohexane ring. The preference of YEH for O-axial C3 epimers, found throughout this study, illustrates the effectiveness of YEH in enzymic detoxification of spiroepoxides.

IT 589-92-4, 4-Methylcyclohexanone
RL: RCT (Reactant); RACT (Reactant or reagent)
(stereochem. preference of yeast epoxide hydrolase for O-axial C3 epimers of 1-oxaspiro[2.5]octanes)

RN 589-92-4 CAPLUS

CN Cyclohexanone, 4-methyl- (CA INDEX NAME)



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 7 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:817105 CAPLUS
DOCUMENT NUMBER: 147:182868
TITLE: Use of DNA microarrays, gene expression profiles, and computer models for predicting cardiotoxicity of substances
INVENTOR(S): Mendrick, Donna L.; Johnson, Kory R.; Daniels, Kellye K.; Porter, Mark W.
PATENT ASSIGNEE(S): Gene Logic, Inc., USA
SOURCE: PCT Int. Appl., 203pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

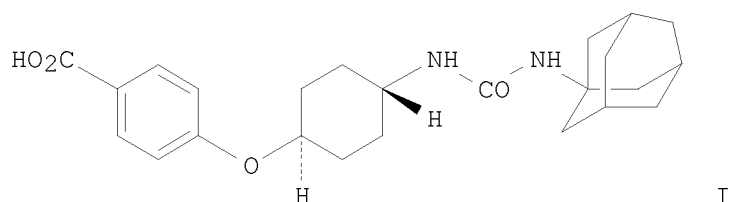
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007084187	A2	20070726	WO 2006-US33712	20060828
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: US 2005-711444P P 20050826
AB The present invention includes methods of predicting cardiotoxicity of test agents and methods of generating cardiotoxicity prediction models using algorithms for analyzing quant. gene expression information. The invention also includes microarrays, computer systems comprising the toxicity prediction models, as well as methods of using the computer systems by remote users for determining the toxicity of test agents.
IT 9015-94-5, Renin, biological studies
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(use of DNA microarrays, gene expression profiles, and computer models for predicting cardiotoxicity of substances)
RN 9015-94-5 CAPLUS
CN Renin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L8 ANSWER 8 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:764736 CAPLUS
DOCUMENT NUMBER: 147:343722
TITLE: Orally Bioavailable Potent Soluble Epoxide Hydrolase Inhibitors
AUTHOR(S): Hwang, Sung Hee; Tsai, Hsing-Ju; Liu, Jun-Yan; Morisseau, Christophe; Hammock, Bruce D.
CORPORATE SOURCE: Department of Entomology and UCD Cancer Center, University of California, Davis, CA, 95616-8584, USA
SOURCE: Journal of Medicinal Chemistry (2007), 50(16),

3825-3840
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 147:343722
 GI



AB A series of N,N'-disubstituted ureas having a conformationally restricted cis- or trans-1,4-cyclohexane α to the urea were prepared and tested as soluble epoxide hydrolase (sEH) inhibitors. This series of compds. showed low nanomolar to picomolar activities against recombinant human sEH. Both isomers showed similar potencies, but the trans isomers were more metabolically stable in human hepatic microsomes. Furthermore, these new potent inhibitors show a greater metabolic stability in vivo than previously described sEH inhibitors. Trans-4-[4-(3-adamantan-1-ylureido)cyclohexyloxy]benzoic acid (I, t-AUCB, IC₅₀ = 1.3 \pm 0.05 nM) had excellent oral bioavailability (98%, n = 2) and blood area under the curve in dogs and was effective in vivo to treat hypotension in lipopolysaccharide challenged murine models.

IT 100-39-0, Benzyl bromide
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of cis and trans isomers of (adamantany lureido)cyclohexanol derivs. as orally bioavailable potent soluble epoxide hydrolase inhibitors)

RN 100-39-0 CAPLUS
 CN Benzene, (bromomethyl)- (CA INDEX NAME)

Ph-CH₂-Br

REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:644048 CAPLUS

DOCUMENT NUMBER: 147:72748

TITLE: Substituted pyrazole compounds useful as soluble epoxide hydrolase inhibitors and their preparation and pharmaceutical compositions

INVENTOR(S): Fleck, Roman Wolfgang; Guo, Xin; Lo, Ho Yin; Man, Chuk Chui

PATENT ASSIGNEE(S): Boehringer Ingelheim International G.m.b.H., Germany; Boehringer Ingelheim Pharma G.m.b.H. & Co. K.-G.

SOURCE: PCT Int. Appl., 317pp.
 CODEN: PIXXD2

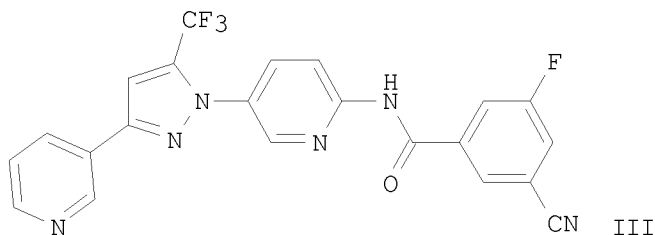
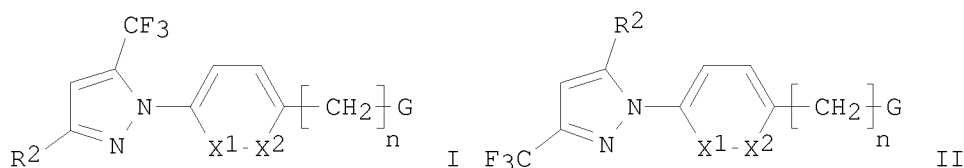
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

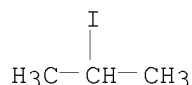
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2007067836	A2	20070614	WO 2006-US60863	20061114
WO 2007067836	A3	20071115		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA			
EP 1960367	A2	20080827	EP 2006-839868	20061114
R:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR			
PRIORITY APPLN. INFO.:			US 2005-742350P	P 20051205
			WO 2006-US60863	W 20061114
OTHER SOURCE(S):	MARPAT 147:72748			
GI				



AB Disclosed are compds. of formula I and II that are active against soluble epoxide hydrolase (sEH), compns. thereof and methods of using and making same. Compds. of formula I and II where G is acylamino; X1-X2 s CH=CH, N=CH, C=N, and N=N; R2 is (un)substituted heteroaryl and (un)substituted carbocycles; n is 0 - 5; and their pharmaceutically acceptable salts thereof, are claimed. Example compound III was prepared by acylation of 3-acetylpyridine with Et trifluoroacetate; the resulting 4,4,4-trifluoro-1-(pyridin-3-yl)butane-1,3-dione underwent cyclization with 2-fluoro-5-hydrazinopyridine to give 2-(6-fluoropyridin-3-yl)-5-(pyridin-3-yl)-3-trifluoromethyl-3,4-dihydro-2H-pyrazol-3-ol, which underwent amination and elimination to give 5-(3-(pyridin-3-yl)-5-trifluoromethylpyrazol-1-yl)pyridin-2-ylamine, which underwent amidation with 3-cyano-5-fluorobenzoic acid to give compound III. All the invention

compds. were evaluated for their sEH inhibitory activity.
IT 75-30-9, 2-Iodopropane
RL: RCT (Reactant); RACT (Reactant or reagent)
(starting material; preparation of substituted pyrazole compds. useful as
soluble epoxide hydrolase inhibitors)
RN 75-30-9 CAPLUS
CN Propane, 2-iodo- (CA INDEX NAME)



L8 ANSWER 10 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:525804 CAPLUS

DOCUMENT NUMBER: 147:157043

TITLE: The role of pharmacogenetics in the metabolism of
antiepileptic drugs: pharmacokinetic and therapeutic
implications

AUTHOR(S): Klotz, Ulrich

CORPORATE SOURCE: Dr Margarete Fischer-Bosch Institut fuer Klinische
Pharmakologie, Stuttgart, Germany

SOURCE: Clinical Pharmacokinetics (2007), 46(4), 271-279
CODEN: CPKNDH; ISSN: 0312-5963

PUBLISHER: Wolters Kluwer Health

DOCUMENT TYPE: Journal; General Review

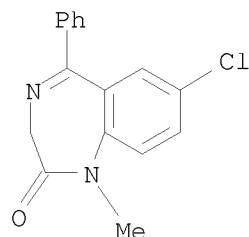
LANGUAGE: English

AB A review. Several different factors, including pharmacogenetics, contribute to inter-individual variability in drug response. Like most other agents, many antiepileptic drugs (AEDs) are metabolized by a variety of enzymic reactions, and the cytochrome P 450 (CYP) superfamily has attracted considerable attention. Some of those CYPs exist in the form of genetic (allelic) variants, which may also affect the plasma concns. or drug exposure (area under the plasma concentration-time curve [AUC]) of AEDs. With regard to the metabolism of AEDs, the polymorphic CYP2C9 and CYP2C19 are of interest. This review summarizes the evidence as to whether such polymorphisms affect the clin. action of AEDs. In the case of mephenytoin, defects in its metabolism may be attributable to >10 mutated alleles (designated as *2, *3 and others) of the gene expressing CYP2C19. Consequently, poor metabolizers (PMs) and extensive metabolizers (EMs) could be differentiated, whose frequencies vary among ethnic populations. CYP2C19 contributes to the metabolism of diazepam and phenytoin, the latter drug also representing a substrate of CYP2C9, with its predominant variants being defined as *2 and *3. For both AEDs, there is maximally a 2-fold difference in the hepatic elimination rate (e.g. clearance) or the AUC between the extremes of EMs and PMs which, in the case of phenytoin (an AED with a narrow 'therapeutic window'), would suggest a dosage reduction only for patients who are carriers of mutated alleles of both CYP2C19 and CYP2C9, a subgroup that is very rare among Caucasians (about 1% of the population) but more frequent in Asians (about 10%). The minor contribution of CYP2C19 to the metabolism of phenobarbital (phenobarbitone) can be overlooked. In rare cases, valproic acid can be metabolized to the reactive (hepatotoxic) metabolite, 4-ene-valproic acid. It is not yet clear whether genetic variants of the involved enzyme (CYP2C9) are responsible for this problem. Likewise, the active metabolite of carbamazepine, carbamazepine-10,11-epoxide, is transformed by the microsomal epoxide hydrolase, an enzyme that is also highly polymorphic, but the pharmacokinetic and clin. consequences still need to be evaluated. Pharmacogenetic investigations have increased our

new general knowledge of drug disposition and action. As for old and especially

AEDs the pharmacogenetic influence on their metabolism is not very striking, it is not surprising that there are no treatment guidelines taking pharmacogenetic data into account. Therefore, the traditional and validated therapeutic drug monitoring approach, representing a direct 'phenotype' assessment, still remains the method of choice when an individualized dosing regimen is anticipated. Nevertheless, pharmacogenetics and pharmacogenomics can offer some novel contributions when attempts are made to maximize drug efficacy and enhance drug safety.

IT 439-14-5, Diazepam
RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(CYP2C9 gene influenced metabolism of diazepam in epileptic patient)
RN 439-14-5 CAPLUS
CN 2H-1,4-Benzodiazepin-2-one, 7-chloro-1,3-dihydro-1-methyl-5-phenyl- (CA INDEX NAME)



REFERENCE COUNT: 64 THERE ARE 64 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 11 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:433827 CAPLUS
DOCUMENT NUMBER: 146:441658
TITLE: Preparation of 2-thienylurea derivatives as inhibitors of soluble epoxide hydrolase
INVENTOR(S): Takahashi, Hitomi; Ota, Tomomi; Kakinuma, Hiroyuki
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 41pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2007043652	A1	20070419	WO 2006-JP320466	20061013
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

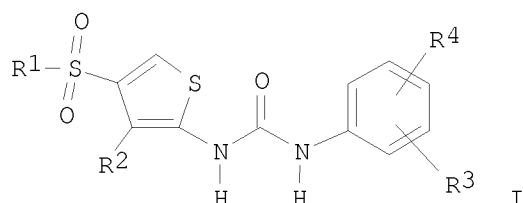
PRIORITY APPLN. INFO.:

JP 2005-299465

A 20051013

OTHER SOURCE(S): MARPAT 146:441658

GI



AB The title compds. I [R1 = alkyl, cycloalkyl, etc.; R2 = H, halo, alkyl; R3, R4 = H, halo, alkyl, alkoxy, etc.] are prepared I are useful in the treatment of hypertension, etc. Thus, 1-[3-chloro-4-(isopropylsulfonyl)-2-thienyl]-3-[3-(trifluoromethyl)phenyl]urea was prepared in several steps from 3-amino-4-(isopropylsulfonyl)thiophene-2-carboxylic acid Et ester. Compds. of this invention showed IC50 values of 0.03 μ M to 0.31 μ M against soluble epoxide hydrolase.

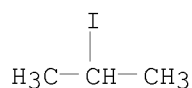
IT 75-30-9, 2-Iodopropane

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of 2-thienylurea derivs. as inhibitors of soluble epoxide hydrolase)

RN 75-30-9 CAPLUS

CN Propane, 2-iodo- (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 12 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:1248277 CAPLUS

DOCUMENT NUMBER: 146:22551

TITLE: Random mutagenesis, screening and selection of protease variants with altered sensitivity to activity modulators

INVENTOR(S): Koltermann, Andre; Kettling, Ulrich; Haupts, Ulrich; Coco, Wayne; Tebbe, Jan; Votsmeier, Christian; Scheidig, Andreas

PATENT ASSIGNEE(S): Direvo Biotech AG, Germany

SOURCE: Eur. Pat. Appl., 93pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

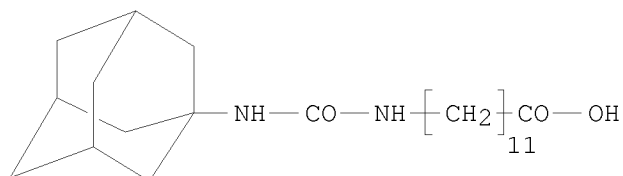
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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EP 1726643	A1	20061129	EP 2005-104543	20050527
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				

US 20060269538 A1 20061130 US 2006-441635 20060526
 WO 2006125827 A1 20061130 WO 2006-EP62644 20060526
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,
 KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,
 MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
 SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,
 VN, YU, ZA, ZM, ZW
 RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
 CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
 GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM
 EP 1883696 A1 20080206 EP 2006-763303 20060526
 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
 IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR
 PRIORITY APPLN. INFO.: EP 2005-104543 A 20050527
 US 2005-685566P P 20050527
 US 2005-686021P P 20050531
 WO 2006-EP62644 W 20060526
 AB The present invention provides a method for the selection of proteases
 with altered sensitivity to one or more activity-modulating substances.
 The method combines the provision of a protease library (i.e., phage
 display library) encoding polynucleotide sequences generated by using PCR
 mutagenesis, expression of the enzymes, screening of the library in the
 presence of one or several activity-modulating substances, selection of
 variants with altered sensitivity to one or several activity-modulating
 substances and isolation of those polynucleotide sequences that encode for
 the selected variants. In particular, mutant variants of human trypsin
 are disclosed.
 IT 9015-94-5P, Renin, biological studies
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);
 PRP (Properties); BIOL (Biological study); PREP (Preparation)
 (random mutagenesis, screening and selection of protease variants with
 altered sensitivity to activity modulators)
 RN 9015-94-5 CAPLUS
 CN Renin (CA INDEX NAME)
 *** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
 REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
 L8 ANSWER 13 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
 ACCESSION NUMBER: 2006:1245497 CAPLUS
 DOCUMENT NUMBER: 146:92622
 TITLE: Design of bioavailable derivatives of
 12-(3-adamantan-1-yl-ureido)dodecanoic acid, a potent
 inhibitor of the soluble epoxide
 hydrolase
 AUTHOR(S): Kim, In-Hae; Nishi, Kosuke; Tsai, Hsing-Ju; Bradford,
 Tanya; Koda, Yasuko; Watanabe, Takaho; Morisseau,
 Christophe; Blanchfield, Joanne; Toth, Istvan;
 Hammock, Bruce D.
 CORPORATE SOURCE: Department of Entomology and University of California
 Davis Cancer Center, University of California, Davis,
 CA, 95616, USA
 SOURCE: Bioorganic & Medicinal Chemistry (2007), 15(1),
 312-323
 CODEN: BMECEP; ISSN: 0968-0896
 PUBLISHER: Elsevier Ltd.

DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 146:92622
 GI



I

AB The soluble epoxide hydrolase (sEH) plays an important role in the metabolism of endogenous chemical mediators involved in blood pressure regulation and vascular inflammation. 12-(3-Adamantan-1-yl-ureido)-dodecanoic acid (AUDA, I) is a very active inhibitor of sEH both in vitro and in vivo. However, its relatively high m.p. and limited solubility in either water or oil-based solvents leads to difficulties in formulating the compound and often results in poor in vivo availability. We investigated the effect of derivatization of the acid functional group of inhibitor I on the inhibition potencies, phys. properties, and pharmacokinetic properties. For human sEH, similar inhibition potency was obtained when the acid of compound I was modified to esters. The resulting compds. exhibited improved phys. properties (23-66°C lower m.p. and 5-fold better solubility in oil). Pharmacokinetic studies showed that the esters possess improved oral bioavailability in mice. On the other hand, amide derivs. of I did not show significant improvement in inhibition potencies or phys. properties (higher m.ps. and lower solubility). The esterification of I results in compds. that are easier to formulate in animal food and in triglycerides for gavage and other routes of administration, making it easier to study the biol. effects of sEH inhibition in vivo.

IT 100-39-0, Benzyl bromide 106-95-6, Allyl bromide, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)
 (bioavailable derivs. of (adamantanylureido)dodecanoic acid as inhibitors of soluble epoxide hydrolase)

RN 100-39-0 CAPLUS

CN Benzene, (bromomethyl)- (CA INDEX NAME)

Ph-CH₂-Br

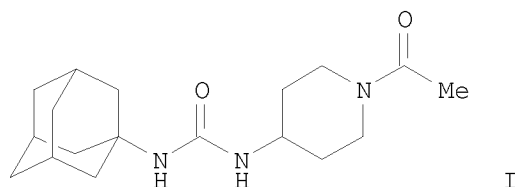
RN 106-95-6 CAPLUS

CN 1-Propene, 3-bromo- (CA INDEX NAME)

Br-CH₂-CH=CH₂

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 14 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:874483 CAPLUS
DOCUMENT NUMBER: 145:454915
TITLE: Synthesis and SAR of conformationally restricted inhibitors of soluble epoxide hydrolase
AUTHOR(S): Jones, Paul D.; Tsai, Hsing-Ju; Do, Zung N.; Morisseau, Christophe; Hammock, Bruce D.
CORPORATE SOURCE: Department of Entomology and Cancer Research Center, University of California, Davis, CA, 95616, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(19), 5212-5216
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:454915
GI



AB A series of conformationally restricted inhibitors of human soluble epoxide hydrolase (sEH) was synthesized. Inhibition potency of the described compds. was studied against recombinant sEH. N-(1-Acetylpiperidin-4-yl)-N'-(adamant-1-yl)urea (I) was found to be a potent inhibitor that was also orally bioavailable in canines.

IT 100-39-0, Benzyl bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation, soluble epoxide hydrolase inhibiting activity, SAR and pharmacokinetics of (N-adamantyl-N'-piperidinyl)urea derivs. using alkylation and acylation of (N-adamantyl-N'-piperidinyl)urea hydrochloride as key steps)

RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)

Ph-CH₂-Br

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 15 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:386356 CAPLUS
DOCUMENT NUMBER: 144:427964
TITLE: Multiple pharmacophore-containing inhibitors for

soluble epoxide hydrolase and
disease treatment

INVENTOR(S): Hammock, Bruce D.; Kim, In-Hae; Morisseau, Christophe;
Watanabe, Takaho; Newman, John W.

PATENT ASSIGNEE(S): The Regents of the University of California, USA

SOURCE: PCT Int. Appl., 179 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006045119	A2	20060427	WO 2005-US38282	20051020
WO 2006045119	A9	20060526		
WO 2006045119	A3	20070208		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM AU 2005295167 A1 20060427 AU 2005-295167 20051020 CA 2584342 A1 20060427 CA 2005-2584342 20051020 US 20060270609 A1 20061130 US 2005-256685 20051020 EP 1814875 A2 20070808 EP 2005-817420 20051020 R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, MK, YU CN 101084216 A 20071205 CN 2005-80043035 20051020 JP 2008517072 T 20080522 JP 2007-538151 20051020 IN 2007KN01641 A 20070817 IN 2007-KN1641 20070508 PRIORITY APPLN. INFO.: US 2004-651487P P 20041020 WO 2005-US38282 W 20051020				

OTHER SOURCE(S): MARPAT 144:427964

AB Inhibitors of the soluble epoxide hydrolase (sEH
) are provided that incorporate multiple pharmacophores and are useful in
the treatment of diseases such as hypertension and inflammation. Thus,
hundreds of inhibitors were synthesized and tested as inhibitors of human
and mouse sEH. The pharmacokinetics of various inhibitors was
also studied.

IT 75-03-6, Ethyl iodide 75-30-9, Isopropyl iodide
100-39-0, Benzyl bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(multiple pharmacophore-containing inhibitors for soluble epoxide
hydrolase and disease treatment)

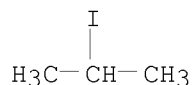
RN 75-03-6 CAPLUS

CN Ethane, iodo- (CA INDEX NAME)

H₃C-CH₂-I

RN 75-30-9 CAPLUS

CN Propane, 2-iodo- (CA INDEX NAME)



RN 100-39-0 CAPLUS

CN Benzene, (bromomethyl)- (CA INDEX NAME)



L8 ANSWER 16 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:358279 CAPLUS

Correction of: 2005:481371

DOCUMENT NUMBER: 145:123921

Correction of: 143:26021

TITLE: Acyclic and cyclic carbonic acids and esters, and their sulfur, selenium, and tellurium analogues

AUTHOR(S): Jung, K. W.; Nagle, A. S.

CORPORATE SOURCE: Dept. of Chemistry, University of South Florida, Tampa, FL, 33620-5250, USA

SOURCE: Science of Synthesis (2005), 18, 379-450

CODEN: SSCYJ9

PUBLISHER: Georg Thieme Verlag

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review of the preparation and synthetic applications of acyclic and cyclic carbonic acids and esters, and their sulfur, selenium, and tellurium analogs.

IT 100-39-0

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation and synthetic applications of acyclic and cyclic carbonic acids and esters, and their sulfur, selenium, and tellurium analogs)

RN 100-39-0 CAPLUS

CN Benzene, (bromomethyl)- (CA INDEX NAME)



L8 ANSWER 17 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:621791 CAPLUS

DOCUMENT NUMBER: 143:286226

TITLE: Stereoselectivity and Substrate Specificity in the Kinetic Resolution of Methyl-Substituted 1-Oxaspiro[2.5]octanes by Rhodotorula glutinis Epoxide Hydrolase

AUTHOR(S): Weijers, Carel A. G. M.; Meeuwse, Petra; Herpers, Robert L. J. M.; Franssen, Maurice C. R.; Sudhoelter, Ernst J. R.

CORPORATE SOURCE: Laboratory of Organic Chemistry, Wageningen University, Wageningen, 6703HB W, Neth.

SOURCE: Journal of Organic Chemistry (2005), 70(17), 6639-6646
CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society

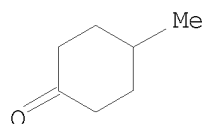
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 143:286226

AB The kinetic resolution of a range of methyl-substituted 1-oxaspiro[2.5]octanes by yeast epoxide hydrolase (YEH) from *Rhodotorula glutinis* has been investigated. The structural determinants of substrate specificity and stereoselectivity of YEH toward these substrates appeared to be the configuration of the epoxide ring and the substitution pattern of the cyclohexane ring. For all compds. tested, O-axial epoxides were hydrolyzed faster than the corresponding O-equatorial compds. In concern of the ring substituents, YEH preferred Me groups on the Re side of the ring. Placement of substituents close to the spiroepoxide carbon decreased the reaction rate but increased enantioselectivity. YEH-catalyzed kinetic resolution of 4-Me 1-oxaspiro[2.5]octane epimers were most enantioselective ($E > 100$).

IT 589-92-4, 4-Methylcyclohexanone
RL: RCT (Reactant); RACT (Reactant or reagent)
(sulfur ylide epoxidn.; stereoselectivity and substrate specificity in the kinetic resolution of methyl-substituted oxaspiro[2.5]octanes by *Rhodotorula glutinis* epoxide hydrolase)

RN 589-92-4 CAPLUS

CN Cyclohexanone, 4-methyl- (CA INDEX NAME)



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:495306 CAPLUS

DOCUMENT NUMBER: 144:128468

TITLE: Solid-phase synthesis of vinyl sulfones using polystyrene-supported selenomethyl phenyl sulfone
AUTHOR(S): Sheng, Shou Ri; Zhou, Wei; Liu, Xiao Ling; Xin, Qin; Song, Cai Sheng

CORPORATE SOURCE: Institutes of Chemistry, Jiangxi Normal University, Nanchang, 330027, Peop. Rep. China

SOURCE: Chinese Chemical Letters (2005), 16(5), 583-584
CODEN: CCLEE7; ISSN: 1001-8417

PUBLISHER: Chinese Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 144:128468

AB The solid-phase preparation of vinyl sulfones via a novel polystyrene-supported selenomethyl Ph sulfone reagent was reported.

IT 100-39-0, Benzyl bromide

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of vinyl sulfones by solid-phase reaction of chloromethylphenylsulfone with primary alkyl halides using polystyrene-supported selenium reagent)

RN 100-39-0 CAPLUS

CN Benzene, (bromomethyl)- (CA INDEX NAME)

Ph-CH₂-Br

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 19 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2005:407002 CAPLUS
Correction of: 2005:155217
DOCUMENT NUMBER: 143:248210
Correction of: 142:240243
TITLE: Product class 2: pyridinones and related systems
AUTHOR(S): Keller, P. A.
CORPORATE SOURCE: Germany
SOURCE: Science of Synthesis (2005), 15, 285-387
CODEN: SSCYJ9
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review of methods to prepare pyridinones and related systems is presented. Synthetic methods include cyclization, aromatization, ring transformation, and substituent modification. The parent pyridinones are generally stable and are easily handled under standard laboratory conditions. The corresponding pyridinethiones are generally more reactive but have the advantage of generally requiring only standard laboratory equipment for their handling. The pyridineselenones are more reactive and the pyridinetellurones have not been comprehensively studied and characterized due to their reactivity and associated difficulty in production

IT 75-03-6 106-95-6, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyridinones and related derivs. via cyclization, aromatization, ring transformation, and substituent modification)

RN 75-03-6 CAPLUS

CN Ethane, iodo- (CA INDEX NAME)

$\text{H}_3\text{C}-\text{CH}_2-\text{I}$

RN 106-95-6 CAPLUS

CN 1-Propene, 3-bromo- (CA INDEX NAME)

$\text{Br}-\text{CH}_2-\text{CH}=\text{CH}_2$

L8 ANSWER 20 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2004:767853 CAPLUS
DOCUMENT NUMBER: 141:410476
TITLE: Polystyrene-supported α -seleno carbanions:
Efficient reagents for highly stereocontrolled
syntheses of vinylphosphonates and vinyl sulfones
AUTHOR(S): Xu, Wei Ming; Tang, E.; Huang, Xian
CORPORATE SOURCE: Department of Chemistry, Zhejiang University,
Hangzhou, 310028, Peop. Rep. China
SOURCE: Synthesis (2004), (13), 2094-2098
CODEN: SYNTBF; ISSN: 0039-7881
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:410476

AB Polystyrene-supported selenomethylphosphonate and polystyrene-supported selenomethyl sulfones have been prepared These novel reagents were treated

with LDA or BuLi to produce polystyrene-supported α -seleno carbanions, which reacted with alkyl halides, followed by stereospecific selenoxide syn-elimination to give E-vinylphosphonates and E-vinyl sulfones resp. Also these novel polymer reagents can be regenerated and reused.

IT 100-39-0, Benzyl bromide 106-95-6, Allyl bromide, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(stereocontrolled synthesis of vinylphosphonates and vinyl sulfones using polystyrene-supported selenomethylphosphonate and selenomethyl sulfone)
RN 100-39-0 CAPLUS
CN Benzene, (bromomethyl)- (CA INDEX NAME)

$\text{Ph}-\text{CH}_2-\text{Br}$

RN 106-95-6 CAPLUS
CN 1-Propene, 3-bromo- (CA INDEX NAME)

$\text{Br}-\text{CH}_2-\text{CH}=\text{CH}_2$

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 21 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:712565 CAPLUS

DOCUMENT NUMBER: 138:470

TITLE: Failure of normal adult Leydig cell development in androgen-receptor-deficient mice

AUTHOR(S): O'Shaughnessy, Peter J.; Johnston, Heather; Willerton, Louise; Baker, Paul J.

CORPORATE SOURCE: Institute of Comparative Medicine, University of Glasgow Veterinary School, Glasgow, G61 1QH, UK

SOURCE: Journal of Cell Science (2002), 115(17), 3491-3496
CODEN: JNCSAI; ISSN: 0021-9533

PUBLISHER: Company of Biologists Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB During testicular development, fetal and adult populations of Leydig cells arise sequentially. Previous studies have shown that androgen action is required for normal steroidogenic activity in the mouse testis. Therefore, to determine the role of androgens in regulating fetal and adult Leydig cell differentiation and function, Leydig development has been measured in mice lacking functional androgen receptors (AR-null). The Leydig cell number was normal on day 5 after birth in AR-null mice but failed to increase normally thereafter and was about 30% of the control level on day 20 and about 60% of control level in adult animals. Levels of 15 different mRNA species expressed specifically in Leydig cells were measured by real-time PCR in AR-null and control animals. Expression levels of all mRNA species were normal on day 5 when only fetal Leydig cells are present. In older animals, which contain predominantly adult Leydig cells, five of the mRNA species (3β -hydroxysteroid dehydrogenase (3β HSD) type 1, cytochrome P 450scc, renin, StAR protein and luteinising hormone receptor) were expressed at normal or increased levels in AR-null mice. All other mRNA species measured showed significantly reduced expression in older animals, and three of these mRNA species (17β -hydroxysteroid dehydrogenase type III, prostaglandin D

(PGD)-synthetase and 3 β HSD type VI), which are only expressed in the adult population of Leydig cells, were barely detectable in the adult AR-null mouse. The results show that in the absence of androgen receptors, fetal Leydig cell function is normal, but there is a developmental failure of adult Leydig cell maturation, with cells only acquiring partial characteristics of the adult population.

IT 9015-94-5, Renin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(androgen receptor role in regulating fetal and adult Leydig cell differentiation and function in development)
RN 9015-94-5 CAPLUS
CN Renin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 22 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:393072 CAPLUS

DOCUMENT NUMBER: 137:216786

TITLE: Asymmetric total synthesis of (+)-exo-brevicommin based on enantioconvergent biocatalytic hydrolysis of an alkene-functionalized 2,3-disubstituted epoxide

AUTHOR(S): Mayer, Sandra F.; Mang, Harald; Steinreiber, Andreas; Saf, Robert; Faber, Kurt

CORPORATE SOURCE: Department of Chemistry, Organic & Bioorganic Chemistry, University of Graz, Graz, A-8010, Austria

SOURCE: Canadian Journal of Chemistry (2002), 80(4), 362-369
CODEN: CJCHAG; ISSN: 0008-4042

PUBLISHER: National Research Council of Canada

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 137:216786

AB A short total asym. synthesis of (+)-exo- and (-)-endo-brevicommin, which are components of the attracting pheromone system of several bark-beetle species belonging to the genera Dendroctonus and Dryocoetes, was accomplished via a chemoenzymic protocol. The key step consisted of biocatalytic hydrolysis by bacterial epoxide hydrolases of cis-configured 2,3-disubstituted oxiranes bearing olefinic side chains. This reaction proceeded in an enantioconvergent fashion, by affording a single enantiomeric vic-diol from the rac-epoxide in up to 92% ee and 83% isolated yield.

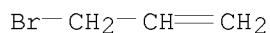
IT 106-95-6, Allyl bromide, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)

(asym. total synthesis of (+)-exo-brevicommin based on enantioconvergent biocatalytic hydrolysis of alkene-functionalized 2,3-disubstituted epoxide)

RN 106-95-6 CAPLUS

CN 1-Propene, 3-bromo- (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 23 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2001:929794 CAPLUS

DOCUMENT NUMBER: 137:89189

TITLE: Identification of novel peroxisome

proliferator-activated receptor α (PPAR α)
target genes in mouse liver using cDNA microarray
analysis

AUTHOR(S): Cherkaoui-Malki, Mustapha; Meyer, Kirstin; Cao,
Wen-Qing; Latruffe, Norbert; Yeldandi, Anjana V.; Rao,
M. Sambasiva; Bradfield, Christopher A.; Reddy,
Janardan K.

CORPORATE SOURCE: Department of Pathology, Northwestern University
Medical School, Chicago, IL, 60611-3008, USA

SOURCE: Gene Expression (2001), 9(6), 291-304
CODEN: GEEXEJ; ISSN: 1052-2166

PUBLISHER: Cognizant Communication Corp.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Peroxisome proliferators, which function as peroxisome
proliferator-activated receptor- α (PPAR α) agonists, are a
group of structurally diverse nongenotoxic hepatocarcinogens including the
fibrate class of hypolipidemic drugs that induce peroxisome proliferation
in liver parenchymal cells. Sustained activation of PPAR α by these
agents leads to the development of liver tumors in rats and mice. To
understand the mol. mechanisms responsible for the pleiotropic effects of
these agents, we have utilized the cDNA microarray to generate a mol.
portrait of gene expression in the liver of mice treated for 2 wk with
Wy-14,643, a potent peroxisome proliferator. PPAR α activation
resulted in the stimulation of expression (fourfold or greater) of 36
genes and decreased the expression (fourfold or more decrease) of 671
genes. Enhanced expression of several genes involved in lipid and glucose
metabolism and many other genes associated with peroxisome biogenesis, cell
surface function, transcription, cell cycle, and apoptosis has been observed
These include: CYP2B9, CYP2B10, monoglyceride lipase, pyruvate
dehydrogenase-kinase-4, cell death-inducing DNA-fragmentation
factor- α , peroxisomal biogenesis factor 11 β , as well as several
cell recognition surface proteins including annexin A2, CD24, CD39,
lymphocyte antigen 6, and retinoic acid early transcript- γ , among
others. Northern blotting of total RNA extracted from the livers of
PPAR α -/- mice and from mice lacking both PPAR α and peroxisomal
fatty acyl-CoA oxidase (AOX), that were fed control and Wy-14,643-containing
diets for 2 wk, as well as time course of induction following a single
dose of Wy-14,643, revealed that upregulation of genes identified by
microarray procedure is dependent upon peroxisome proliferation vis-a-vis
PPAR α . However, cell death-inducing DNA-fragmentation
factor- α mRNA, which is increased in the livers of wild-type mice
treated with peroxisome proliferators, was not enhanced in AOX-/- mice
with spontaneous peroxisome proliferation. These observations indicate
that the activation of PPAR α leads to increased and decreased
expression of many genes not associated with peroxisomes, and that delayed
onset of enhanced expression of some genes may be the result of metabolic
events occurring secondary to PPAR α activation and alterations in
lipid metabolism

IT 9015-94-5, Renin, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(identification of peroxisome proliferator-activated receptor α
(PPAR α) target genes in mouse liver using cDNA microarray anal.)

RN 9015-94-5 CAPLUS

CN Renin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 2001:338762 CAPLUS
 DOCUMENT NUMBER: 134:362292
 TITLE: Methods of determining individual hypersensitivity to
 a pharmaceutical agent from gene expression profile
 INVENTOR(S): Farr, Spencer
 PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
 SOURCE: PCT Int. Appl., 222 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103
WO 2001032928	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
 CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
 HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
 LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
 YU, ZA, ZW

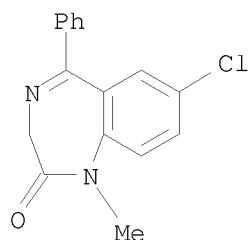
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398P P 19991105
 US 2000-196571P P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein
 arrays, and devices that may be used to determine the hypersensitivity of
 individuals to a given agent, such as drug or other chemical, in order to
 prevent toxic side effects. In one embodiment, methods of identifying
 hypersensitivity in a subject by obtaining a gene expression profile of
 multiple genes associated with hypersensitivity of the subject suspected to
 be hypersensitive, and identifying in the gene expression profile of the
 subject a pattern of gene expression of the genes associated with
 hypersensitivity are disclosed. The gene expression profile of the
 subject may be compared with the gene expression profile of a normal
 individual and a hypersensitive individual. The gene expression profile
 of the subject that is obtained may comprise a profile of levels of mRNA
 or cDNA. The gene expression profile may be obtained by using an array of
 nucleic acid probes for the plurality of genes associated with
 hypersensitivity. The expression of the genes predetd. to be associated with
 hypersensitivity is directly related to prevention or repair of toxic
 damage at the tissue, organ or system level. Gene databases arrays and
 apparatus useful for identifying hypersensitivity in a subject are also
 disclosed.

IT 439-14-5, Diazepam
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); BIOL (Biological study)
 (methods of determining individual hypersensitivity to a pharmaceutical
 agent
 from gene expression profile)

RN 439-14-5 CAPLUS
 CN 2H-1,4-Benzodiazepin-2-one, 7-chloro-1,3-dihydro-1-methyl-5-phenyl- (CA
 INDEX NAME)



L8 ANSWER 25 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:326455 CAPLUS

DOCUMENT NUMBER: 131:208530

TITLE: A multi-laboratory evaluation of cryopreserved monkey hepatocyte functions for use in pharmaco-toxicology

AUTHOR(S): de Sousa, Georges; Nicolas, Florence; Placidi, Michel; Rahmani, Roger; Benicourt, Marc; Vannier, Bernard; Lorenzon, Giocondo; Mertens, Karine; Coecke, Sandra; Callaerts, Andre; Rogiers, Vera; Khan, Shamas; Roberts, Phil; Skett, Paul; Fautrel, Alain; Chesne, Christophe; Guillouzo, Andre

CORPORATE SOURCE: INSERM/Centre de Recherche Agronomique, Antibes, 06606, Fr.

SOURCE: Chemico-Biological Interactions (1999), 121(1), 77-97
CODEN: CBINA8; ISSN: 0009-2797

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

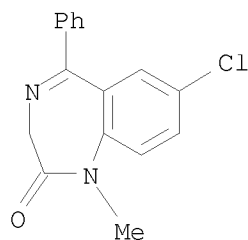
AB Ethical, economic and tech. reasons hinder regular supply of freshly isolated hepatocytes from higher mammals such as monkey for preclin. evaluation of drugs. Hence, the authors aimed at developing optimal and reproducible protocols to cryopreserve and thaw parenchymal liver cells from this major toxicol. species. Before the routine use of these protocols, the authors validated them through a multi-laboratory study. Dissociation of the whole animal liver resulted in obtaining 1-5 billion parenchymal cells with a viability of about 86%. An appropriate fraction (around 20%) of the freshly isolated cells was immediately set in primary culture and various hepato-specific tests were performed to examine their metabolic, biochem. and toxicol. functions as well as their ultrastructural characteristics. The major part of the hepatocytes was frozen and their functionality checked using the same parameters after thawing. The characterization of fresh and thawed monkey hepatocytes demonstrated the maintenance of various hepato-specific functions. Indeed, cryopreserved hepatocytes were able to survive and to function in culture as well as their fresh counterparts. The ability for synthesis (proteins, ATP, GSH) and conjugation and secretion of biliary acids was preserved after deep freeze storage. A better stability of drug metabolizing activities than in rodent hepatocytes was observed in monkey. After thawing, Phase I and Phase II activities (cytochrome P 450, ethoxycoumarin-O-deethylase, aldrin epoxidase, epoxide hydrolase, glutathione transferase, glutathione reductase and glutathione peroxidase) were well preserved. The metabolic patterns of several drugs were qual. and quant. similar before and after cryopreservation. Lastly, cytotoxicity tests suggested that the freezing/thawing steps did not change cell sensitivity to toxic compds.

IT 439-14-5, Diazepam

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(metabolism; multi-laboratory evaluation of cryopreserved monkey hepatocyte functions for use in pharmaco-toxicol. in relation to drug metabolism)

RN 439-14-5 CAPLUS
CN 2H-1,4-Benzodiazepin-2-one, 7-chloro-1,3-dihydro-1-methyl-5-phenyl- (CA
INDEX NAME)



REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 26 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1997:415295 CAPLUS

DOCUMENT NUMBER: 127:130797

ORIGINAL REFERENCE NO.: 127:25089a,25092a

TITLE: In vivo induction and in vitro inhibition of hepatic
cytochrome P450 activity by the benzodiazepine
anticonvulsants clonazepam and diazepam

AUTHOR(S): Nims, Raymond W.; Prough, Russell A.; Jones, Collins
R.; Stockus, Diana L.; Dragnev, Konstantin H.; Thomas,
Paul E.; Lubet, Ronald A.

CORPORATE SOURCE: Chemistry Section, Laboratory of Comparative
Carcinogenesis and Biological Carcinogenesis and
Development Program, National Cancer Inst., USA

SOURCE: Drug Metabolism and Disposition (1997), 25(6), 750-756
CODEN: DMDSAI; ISSN: 0090-9556

PUBLISHER: Williams & Wilkins

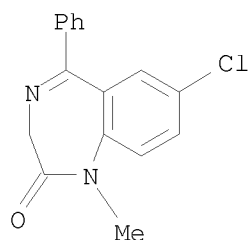
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The ability of the benzodiazepines, as a chemical class, to cause the
induction and/or inhibition of cytochromes P 450 has not been well
characterized. In the present study, the induction of the cytochrome P
450 2B subfamily (CYP2B) in vivo and the inhibition of CYP2B activity in
vitro by selected benzodiazepines was examined in hepatic tissues derived
from male F344/NCr rats. Initial studies of the in vivo induction or in
vitro inhibition of benzyloxyresorufin O-dealkylation activity revealed
that both clonazepam and diazepam were relatively effective in vivo
inducers of CYP2B when administered in the diet at 500 ppm for 5 days and
also were fairly potent inhibitors of the activity of these hemoproteins
in vitro. Oxazepam, in contrast, was ineffective as an inducer or an
inhibitor of this activity. Further studies were performed to
characterize the subfamily selectivity of the P 450 induction and
inhibition displayed by clonazepam. Specifically, microsomes from rats
treated with clonazepam (1000 or 1800 ppm in the diet for 5 days) were
found to be highly induced with respect to catalytic activities mediated
by CYP2B, including benzyloxyresorufin and pentoxyresorufin O-dealkylation
or testosterone 16 β -hydroxylation, but other CYP proteins were
minimally induced. In addition to inducing the CYP2B subfamily, clonazepam
also induced the RNA encoding other drug metabolizing enzymes (e.g.,
epoxide hydrolase and the glutathione S-transferase
 α -subfamily) that are typically induced by phenobarbital-type
inducers. Finally, clonazepam proved to be a potent noncompetitive or
"mixed-type" competitive inhibitor of catalytic activities mediated by
CYP2B, but not by other CYP proteins (e.g. CYP2A, CYP3A) in microsomes

derived from phenobarbital-pretreated rats.

IT 439-14-5, Diazepam
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(benzodiazepine anticonvulsants induction and inhibition of hepatic cytochrome P 450 activity)
RN 439-14-5 CAPLUS
CN 2H-1,4-Benzodiazepin-2-one, 7-chloro-1,3-dihydro-1-methyl-5-phenyl- (CA INDEX NAME)



L8 ANSWER 27 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:465674 CAPLUS
DOCUMENT NUMBER: 125:161867
ORIGINAL REFERENCE NO.: 125:30167a,30170a
TITLE: Regioselectivity of Rhodococcus NCIMB 11216
epoxide hydrolase: applicability of
E-values for description of enantioselectivity depends
on substrate structure
AUTHOR(S): Mischitz, M.; Mirtl, C.; Saf, R.; Faber, K.
CORPORATE SOURCE: Inst. of Organic Chemistry, Graz Univ. of Technology,
Graz, A-8010, Austria
SOURCE: Tetrahedron: Asymmetry (1996), 7(7), 2041-2046
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 125:161867
AB The regioselectivity of purified epoxide hydrolase
from Rhodococcus NCIMB 11216 was investigated by hydrolyzing a series of
structurally different epoxides 1a-5a in 18O-labeled water followed by
GC/MS anal. of the 1,2-diols formed 1b-5b. The enzyme introduced a single
18O-atom in a trans-specific fashion with a varying degree of
regioselectivity depending on the substitution pattern of the substrate.
With an aliphatic mono-1a and 2,2-disubstituted oxirane 3a the attack
occurred exclusively at the less hindered C-atom and complete retention of
configuration was retained. The regioselectivity was low with a 2,3-di-4a
and a trisubstituted epoxide 5a, and with a substrate bearing a benzylic
oxirane atom 2a. As a consequence, the 'Enantiomeric Ratio' (E) can be
applied to describe the selectivity of kinetic resolns. for some, but not
for all types of substrates.
IT 75-03-6, Ethyl iodide
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant for preparation of epoxide hydrolase
substrates and products)
RN 75-03-6 CAPLUS
CN Ethane, iodo- (CA INDEX NAME)

H₃C-CH₂-I

L8 ANSWER 28 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1994:455036 CAPLUS

DOCUMENT NUMBER: 121:55036

ORIGINAL REFERENCE NO.: 121:9891a

TITLE: Enhanced blood pressure response to mineralocorticoid stimulation in normotensive members of hypertensive families

AUTHOR(S): Ferrari, Paolo; Travaglini, Marco; Schild, Christoph; Allemann, Yves; Shaw, Sidney; Weidmann, Peter

CORPORATE SOURCE: Med. Poliklin., Univ. Berne, Switz.

SOURCE: Blood Pressure (1992), 1(2), 86-91

CODEN: BLPREG; ISSN: 0803-7051

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Currently normotensive offspring of essential hypertensive parents often have disturbances in blood pressure (BP) regulation such as abnormalities in electrolyte homeostasis, increased salt-sensitivity and/or impaired renal Na⁺-excretion. Whether an altered reactivity to mineralocorticoids may also play a role is presently unknown. Therefore, the authors investigated BP (recorded during 24 h), plasma atrial natriuretic factor (ANF), cyclic guanosine monophosphate (cGMP), aldosterone (PA) and renin activity (PRA), 24-h urine electrolyte and cGMP excretions measured on 4 consecutive days, as well as other variables, after 1 wk on placebo and after 3 wk of 9 α -fludrocortisoneacetate (9 α F) administration, 0.6 mg/d in 12 normotensive sons of essential hypertensive parents (SEH) and 12 body-mass-index- and age-matched (25 \pm 1[\pm SEM]yr) sons of normotensive parents (SN). On placebo, the 2 groups did not differ significantly in average 24 h BP (mean BP 95 \pm 2 mmHg), plasma-ANF (40 \pm 7 vs 30 \pm 5 pg/mL), cGMP (6 \pm 0.4 vs 6 \pm 0.5 nmol/L), PRA (1.3 \pm 0.1 vs 1.6 \pm 0.2 ng/mL/h), PA (9 \pm 0.5 vs 10 \pm 0.9 ng/dL), hematocrit (44 \pm 0.7 vs 44 \pm 0.4%) and 96-h urinary-Na⁺ (mean 205 \pm 13 vs 195 \pm 16 mmol/d), -K⁺ (69 \pm 6 vs 78 \pm 7 mmol/d) or -cGMP (461 \pm 35 vs 483 \pm 32 nmol/d). 9 α F significantly increased BP in SEH (p<0.005) but not SN (107 \pm 2 vs 100 \pm 2 mmHg, p<0.05). Elevation of BP during the night accounted for this difference (+13 vs +8 mmHg, p<0.02). However, during 9 α F the 2 groups did not differ with regard of plasma ANF (106 \pm 13 vs 100 \pm 14 pg/mL), cGMP (10 \pm 1.1 vs 10 \pm 1.4 nmol/L), PRA (0.5 \pm 0.1 vs 0.5 \pm 0.2 ng/mL/h), PA (5 \pm 0.3 vs 4 \pm 0.3 ng/dL), 96-h urinary-Na⁺ (205 \pm 19 vs 195 \pm 17 mmol/d), -K⁺ (80 \pm 8 vs 69 \pm 6 mmol/d) or -cGMP (673 \pm 76 vs 653 \pm 62 nmol/d), plasma-Na⁺ (increase +3 vs +2 mmol/L), K⁺ (decrease -0.5 vs -0.5 mmol/L), hematocrit (42 \pm 0.8 vs 42 \pm 0.2%) or body weight (increase +2.0 vs +1.9 kg). These results indicate that normotensive offspring of hypertensive parents may react to mineralocorticoid stimulation with an enhanced BP-increase. This disturbance cannot be explained by insufficient renin-aldosterone suppression, inadequate ANF stimulation or abnormally increased Na⁺-fluid retention.

IT 9015-94-5, Renin, biological studies

RL: BIOL (Biological study)

(in plasma of normotensive sons from essential hypertensive families, enhanced blood pressure response to mineralocorticoid in relation to)

RN 9015-94-5 CAPLUS

CN Renin (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L8 ANSWER 29 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1990:21032 CAPLUS

DOCUMENT NUMBER: 112:21032

ORIGINAL REFERENCE NO.: 112:3695a,3698a

TITLE: Boron compounds. 87. 1,5-Cyclooctanediylboryl selenides - preparation, characterization, and application

AUTHOR(S): Koester, Roland; Seidel, Guenter; Yalpani, Mohamed

CORPORATE SOURCE: Max-Planck-Inst. Kohlenforsch., Muelheim an der Ruhr, D-4330, Fed. Rep. Ger.

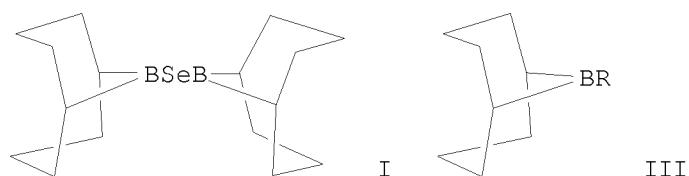
SOURCE: Chemische Berichte (1989), 122(10), 1815-24
CODEN: CHBEAM; ISSN: 0009-2940

DOCUMENT TYPE: Journal

LANGUAGE: German

OTHER SOURCE(S): CASREACT 112:21032

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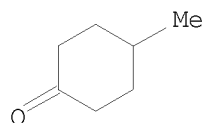


AB Bis(1,5-cyclooctanediylboryl) selenide (I) is prepared quant. from bis(9-borabicyclo[3.3.1]nonane) (BBN)₂ and Se in mesitylene at 150°, and the corresponding diselenide (II) is prepared by reaction of I with Se in mesitylene at 120°. I reacts with aniline to give BBN derivs. III (R = SeH, NPh). Reactions of I with γ-picoline, Me₃P, trialkoxyboranes, alkynes, Fe₂O₃, and other compds. are also examined, along with reactions of II and III (R = SeH).

IT 589-92-4, 4-Methylcyclohexanone
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with cyclooctanediylboryl selenides)

RN 589-92-4 CAPLUS

CN Cyclohexanone, 4-methyl- (CA INDEX NAME)



L8 ANSWER 30 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1977:189112 CAPLUS

DOCUMENT NUMBER: 86:189112

ORIGINAL REFERENCE NO.: 86:29653a,29656a

TITLE: The unsaturated esters of diselenophosphoric acid

AUTHOR(S): Zemlyanskii, N. L.; Mel'nik, Ya. G.; Turkevich, V. V.; Makota, I. P.; Koretskii, A. S.

CORPORATE SOURCE: USSR

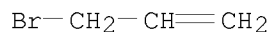
SOURCE: Visnik L'vivs'kogo Derzhavnogo Universitetu, Seriya Khimichna (1975), 17, 65-8
CODEN: VLDUAB; ISSN: 0460-0509

DOCUMENT TYPE: Journal

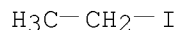
LANGUAGE: Ukrainian

AB (RO)₂P(Se)SeH (R = Et, Pr, Me₂CH, Bu) were neutralized with K₂CO₃ and then treated with R₁Br (R₁ = allyl, HC.tplbond.CCH₂) in Me₂CO at 40° to give 71-82% (RO)₂P(Se)SeR₁ (I). Mol. association was deduced

from the IR spectra of all 4 I (R1 = CH2C.tplbond.CH).
IT 106-95-6, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation of dialkyl diselenophosphates with)
RN 106-95-6 CAPLUS
CN 1-Propene, 3-bromo- (CA INDEX NAME)



L8 ANSWER 31 OF 31 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1938:63839 CAPLUS
DOCUMENT NUMBER: 32:63839
ORIGINAL REFERENCE NO.: 32:8937i,8938a
TITLE: Raman effect. LXXXVI. Ethyl derivatives
AUTHOR(S): Wagner, J.
SOURCE: Z. physik. Chem. (1938), B40, 439-49
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C. A. 32, 6549.5. Raman spectra were obtained for EtX, where X = OH, SH, Cl and I. Results of other investigations, where X = Me, NH2, Br and SeH have been included in the calcns. The mols. have been treated as a 3-particle system with a valence force potential energy function. The calculated vibrational frequencies agree with experiment only if the atomic weight of X is less than 36. The valence force consts. are smaller and the nuclear distances are larger than those for the corresponding methyl derivs.
IT 75-03-6, Ethane, iodo-
(Raman spectrum of)
RN 75-03-6 CAPLUS
CN Ethane, iodo- (CA INDEX NAME)



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